

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
12 December 2002 (12.12.2002)

PCT

(10) International Publication Number
WO 02/098358 A2

- (51) International Patent Classification⁷: **A61K**
- (21) International Application Number: PCT/US02/17594
- (22) International Filing Date: 4 June 2002 (04.06.2002)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:
- | | | |
|------------|-------------------------------|----|
| 60/295,917 | 4 June 2001 (04.06.2001) | US |
| 60/350,666 | 13 November 2001 (13.11.2001) | US |
| 60/368,689 | 29 March 2002 (29.03.2002) | US |
| 60/372,246 | 12 April 2002 (12.04.2002) | US |
| 10/160,233 | 31 May 2002 (31.05.2002) | US |
- (71) Applicant: **EOS BIOTECHNOLOGY, INC.** [US/US];
225A Gateway Boulevard, South San Francisco, CA 94080 (US).
- (72) Inventors: **AFAR, Daniel, E., H.**; 435 Visitation Avenue, Brisbane, CA 94005 (US). **AGUS, David**; 522 North Crescent Drive, Beverly Hills, CA 90210 (US). **MACK, David, H.**; 2076 Monterey Avenue, Menlo Park, CA 94025 (US).
- (74) Agents: **BASTIAN, Kevin, L.** et al.; Townsend and Townsend and Crew LLP, Two Embarcadero Center, Eighth Floor, San Francisco, CA 94111 (US).
- (81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW.
- (84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CR, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— without international search report and to be republished upon receipt of that report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 02/098358 A2

(54) Title: METHODS OF DIAGNOSIS AND TREATMENT OF ANDROGEN-DEPENDENT PROSTATE CANCER, PROSTATE CANCER UNDERGOING ANDROGEN-WITHDRAWAL, AND ANDROGEN-INDEPENDENT PROSTATE CANCER

(57) Abstract: Described herein are genes whose expression are up-regulated or down-regulated in prostate cancer. Also described are such genes whose expression is further up-regulated or down-regulated in drug-resistant prostate cancer cells. Related methods and compositions that can be used for diagnosis and treatment of prostate cancer are disclosed. Also described herein are methods that can be used to identify modulators of prostate cancer.

METHODS OF DIAGNOSIS AND TREATMENT OF ANDROGEN-DEPENDENT PROSTATE CANCER, PROSTATE CANCER UNDERGOING ANDROGEN WITHDRAWAL, AND ANDROGEN-INDEPENDENT PROSTATE CANCER

5

CROSS-REFERENCES TO RELATED APPLICATIONS

This application claims priority from the following applications: USSN 60/295,917, filed June 4, 2001, USSN 60/368,689, filed March 29, 2002; USSN 60/350,666, filed November 13, 2001; and USSN 60/372,246, filed April 12, 2002; each of which is incorporated herein by reference in its entirety.

10

FIELD OF THE INVENTION

The invention relates to the identification of nucleic acid and protein expression profiles and nucleic acids, products, and antibodies thereto that are involved in prostate cancer; and to the use of such expression profiles and compositions in the diagnosis, prognosis, and therapy of prostate cancer. The invention further relates to methods for identifying and using agents and/or targets that inhibit prostate cancer.

15

BACKGROUND OF THE INVENTION

Prostate cancer is the most frequently diagnosed cancer and the second leading cause of male cancer death in North America and northern Europe. Early detection of prostate cancer using a serum test for prostate-specific antigen (PSA) has dramatically improved the treatment of the disease (Oesterling (1992) J. Am. Med. Assoc., 267:2236-2238). Treatment of prostate cancer consists largely of surgical prostatectomy, radiation therapy, androgen ablation therapy and chemotherapy. Although many prostate cancer patients are effectively treated, the current therapies can all induce serious side effects which diminish quality of life. Patients who present with metastatic disease are most often treated with androgen-ablation therapy. Hormone blockade results in significant regression of the tumor. However, this treatment rarely cures the patient and invariably results in progression to androgen-

20

25

independent disease, which is incurable. Afrin and Stuart (1994) J.S.C. Med. Assoc. 90:231-236.

The identification of novel therapeutic targets and diagnostic markers is essential for improving the current treatment of prostate cancer patients. Recent advances in molecular medicine have increased the interest in tumor-specific cell surface antigens that could serve as targets for various immunotherapeutic or small molecule strategies. Antigens suitable for immunotherapeutic strategies should be highly expressed in cancer tissues and ideally not expressed in normal adult tissues. Expression in tissues that are dispensable for life, however, may be tolerated. Examples of such antigens include Her2/neu and the B-cell antigen CD20. Humanized monoclonal antibodies directed to Her2/neu (Herceptin) are currently in use for the treatment of metastatic breast cancer. Ross and Fletcher (1998) Stem Cells 16:413-428. Similarly, anti-CD20 monoclonal antibodies (Rituxin) are used to effectively treat non-Hodgkin's lymphoma. Maloney, et al. (1997) Blood 90:2188-2195; Leget and Czuczman (1998) Curr. Opin. Oncol. 10:548-551.

Several potential immunotherapeutic targets have been identified for prostate cancer. They include prostate-specific membrane antigen (PSMA) (Israeli, et al. (1993) Cancer Res. 53:227-230), prostate stem cell antigen (PSCA; Reiter, et al. (1998) Proc. Natl. Acad. Sci. USA 95:1735-1740), and serpentine transmembrane epithelial antigen of the prostate (STEAP; Hubert, et al. (1999) Proc. Natl. Acad. Sci. USA 96:14529-14534). PSMA is a type II transmembrane hydrolase with significant homology to a rat neuropeptidase (Carter, et al. (1996) Proc. Natl. Acad. Sci. USA 93:749-753). Antibodies directed towards PSMA are currently being used to detect metastasized prostate cancer as the Proscint Scan (Sodee, et al. (1996) Clin. Nucl. Med. 21:759-767) and are also being evaluated for treatment of advanced disease (Gregorakis, et al. (1998) Semin. Urol. Oncol. 16:2-12; Liu, et al. (1998) Cancer Res. 58:4055-4060; Murphy, et al. (1998) J. Urol. 160:2396-2401). In a study on bone metastasis of prostate cancer, only 8 out of 18 patient samples expressed PSMA (Silver, et al. (1997) Clin. Cancer Res. 3:81-85). Therefore, it is clear that other targets need to be identified to manage metastasized disease. PSCA is a member of the Thy-1/Ly-6 family of glycosylphosphatidylinositol-linked plasma membrane proteins (Reiter, et al. (1998) Proc. Natl. Acad. Sci. USA 95:1735-1740). Immunohistochemical data shows that PSCA is up-regulated in the majority of prostate cancer epithelia and is also detected in bone metastasis (Gu, et al. (2000) Oncogene 19:1288-1296). Recent work shows that antibodies directed to

PSCA can prevent metastatic spread of prostate cancer in a mouse model (Saffran, et al. (2001) Proc. Natl. Acad. Sci. USA 98:2658-2663). STEAP is a multi-transmembrane prostate-specific protein that may function as a channel or transporter protein (Hubert, et al. (1999) Proc. Natl. Acad. Sci. USA 96:14529-14534). Its protein expression is specific to the basolateral membranes of normal prostate and prostate cancer epithelia. STEAP expression was most highly concentrated at cell-cell boundaries, implying a potential function in intercellular communication. Therapeutic monoclonal antibodies have so far not been reported for STEAP.

SUMMARY OF THE INVENTION

The present invention therefore provides nucleotide sequences of genes that are up- and down-regulated in androgen-independent prostate cancer cells or prostate cells undergoing androgen withdrawal. Such genes are useful for diagnostic purposes, and also as targets for screening for therapeutic compounds that modulate prostate cancer, such as hormones or antibodies. Other aspects of the invention will become apparent to the skilled artisan by the following description of the invention.

In one aspect, the present invention provides a method of detecting an androgen independent prostate cancer-associated transcript in a cell from a patient, the method comprising contacting a biological sample from the patient with a polynucleotide that selectively hybridizes to nucleic acid molecule comprising a sequence at least 80% identical to a sequence as shown in Tables 1A-4.

In one embodiment, the present invention provides a method of determining the level of a prostate cancer associated transcript in a cell from a patient.

In one embodiment, the present invention provides a method of detecting a prostate cancer-associated transcript in a cell from a patient, the method comprising contacting a biological sample from the patient with a polynucleotide that selectively hybridizes to a sequence at least 80% identical to a sequence as shown in Tables 1A-4.

In various embodiments, the polynucleotide selectively hybridizes to a sequence at least 95% identical to a sequence as shown in Tables 1A-4; the polynucleotide comprises a sequence as shown in Tables 1A-4; the biological sample is a tissue sample; the biological sample comprises isolated nucleic acids, e.g., mRNA; the polynucleotide is labeled, e.g., with a fluorescent label; the polynucleotide is immobilized on a solid surface; the patient is

undergoing a therapeutic regimen to treat prostate cancer; the patient is suspected of having metastatic prostate cancer; the patient is a human; the patient is suspected of having a taxol-resistant cancer; or the prostate cancer associated transcript is mRNA.

In other embodiments, the method further comprises the step of amplifying nucleic acids before the step of contacting the biological sample with the polynucleotide.

In another aspect, the present invention provides a method of monitoring the efficacy of a therapeutic treatment of prostate cancer, the method comprising the steps of: (i) providing a biological sample from a patient undergoing the therapeutic treatment; and (ii) determining the level of a prostate cancer-associated transcript in the biological sample by contacting the biological sample with a polynucleotide that selectively hybridizes to a sequence at least 80% identical to a sequence as shown in Tables 1A-4, thereby monitoring the efficacy of the therapy. In a further embodiment, the patient has metastatic prostate cancer. In a further embodiment, the patient has a drug resistant (e.g., taxol resistant) form of prostate cancer.

In one embodiment, the method further comprises the step of: (iii) comparing the level of the prostate cancer-associated transcript to a level of the prostate cancer-associated transcript in a biological sample from the patient prior to, or earlier in, the therapeutic treatment.

Additionally, provided herein is a method of evaluating the effect of a candidate prostate cancer drug comprising administering the drug to a patient and removing a cell sample from the patient. The expression profile of the cell is then determined. This method may further comprise comparing the expression profile to an expression profile of a healthy individual. In a preferred embodiment, said expression profile includes a gene of Tables 1A-4.

In one aspect, the present invention provides an isolated nucleic acid molecule consisting of a polynucleotide sequence as shown in Tables 1A-4.

In one embodiment, an expression vector or cell comprises the isolated nucleic acid.

In one aspect, the present invention provides an isolated polypeptide which is encoded by a nucleic acid molecule having polynucleotide sequence as shown in Tables 1A-4.

In another aspect, the present invention provides an antibody that specifically binds to an isolated polypeptide which is encoded by a nucleic acid molecule having polynucleotide sequence as shown in Tables 1A-4.

In certain embodiments, the antibody is conjugated to an effector component, e.g., a fluorescent label, a radioisotope or a cytotoxic chemical; the antibody is an antibody fragment; or the antibody is humanized.

In one aspect, the present invention provides a method of detecting a prostate cancer cell in a biological sample from a patient, the method comprising contacting the biological sample with an antibody as described herein.

In another aspect, the present invention provides a method of detecting antibodies specific to prostate cancer in a patient, the method comprising contacting a biological sample from the patient with a polypeptide encoded by a nucleic acid comprising a sequence from
10 Tables 1A-4.

In another aspect, the present invention provides a method for identifying a compound that modulates a prostate cancer-associated polypeptide, the method comprising the steps of:
a) contacting the compound with a prostate cancer-associated polypeptide, the polypeptide encoded by a polynucleotide that selectively hybridizes to a sequence at least 80% identical
15 to a sequence as shown in Tables 1A-4; and b) determining the functional effect of the compound upon the polypeptide.

In one embodiment, the functional effect is a physical effect, an enzymatic effect, or a chemical effect.

In one embodiment, the polypeptide is expressed in a eukaryotic host cell or cell
20 membrane. In another embodiment, the polypeptide is recombinant.

In one embodiment, the functional effect is determined by measuring ligand binding to the polypeptide.

In another aspect, the present invention provides a method of inhibiting proliferation of a prostate cancer-associated cell to treat prostate cancer in a patient, the method
25 comprising the step of administering to the subject a therapeutically effective amount of a compound identified as described herein.

In one embodiment, the compound is an antibody.

In another aspect, the present invention provides a drug screening assay comprising the steps of: a) administering a test compound to a mammal having prostate cancer or to a
30 cell sample isolated therefrom; b) comparing the level of gene expression of a polynucleotide that selectively hybridizes to a sequence at least 80% identical to a sequence as shown in Tables 1A-4 in a treated cell or mammal with the level of gene expression of the

polynucleotide in a control cell sample or mammal, wherein a test compound that modulates the level of expression of the polynucleotide is a candidate for the treatment of prostate cancer.

5 In one embodiment, the control is a mammal with prostate cancer or a cell sample therefrom that has not been treated with the test compound. In another embodiment, the control is a normal cell or mammal.

In one embodiment, the test compound is administered in varying amounts or concentrations. In another embodiment, the test compound is administered for varying time periods. In another embodiment, the comparison can occur after addition or removal of the
10 drug candidate.

In one embodiment, the levels of a plurality of polynucleotides that selectively hybridize to a sequence at least 80% identical to a sequence as shown in Tables 1A-4 are individually compared to their respective levels in a control cell sample or mammal. In a preferred embodiment the plurality of polynucleotides is from three to ten.

15 In another aspect, the present invention provides a method for treating a mammal having prostate cancer comprising administering a compound identified by the assay described herein.

In another aspect, the present invention provides a pharmaceutical composition for treating a mammal having prostate cancer, the composition comprising a compound
20 identified by the assay described herein and a physiologically acceptable excipient.

In one aspect, the present invention provides a method of screening drug candidates by providing a cell expressing a gene that is up- and down-regulated as in a prostate cancer. In one embodiment, a gene is selected from Tables 1A-4. The method further includes adding a drug candidate to the cell and determining the effect of the drug candidate on the
25 expression of the expression profile gene.

In one embodiment, the method of screening drug candidates includes comparing the level of expression in the absence of the drug candidate to the level of expression in the presence of the drug candidate, wherein the concentration of the drug candidate can vary when present, and wherein the comparison can occur after addition or removal of the drug
30 candidate. In a preferred embodiment, the cell expresses at least two expression profile genes. The profile genes may show an increase or decrease.

Also provided is a method of evaluating the effect of a candidate prostate cancer drug comprising administering the drug to a transgenic animal expressing or over-expressing the prostate cancer modulatory protein, or an animal lacking the prostate cancer modulatory protein, for example as a result of a gene knockout.

- 5 Moreover, provided herein is a biochip comprising one or more nucleic acid segments of Tables 1A-4, wherein the biochip comprises fewer than 1000 nucleic acid probes. Preferably, at least two nucleic acid segments are included. More preferably, at least three nucleic acid segments are included.

- 10 Furthermore, a method of diagnosing a disorder associated with prostate cancer is provided. The method comprises determining the expression of a gene of Tables 1A-4, in a first tissue type of a first individual, and comparing the distribution to the expression of the gene from a second normal tissue type from the first individual or a second unaffected individual. A difference in the expression indicates that the first individual has a disorder associated with prostate cancer.

- 15 In a further embodiment, the biochip also includes a polynucleotide sequence of a gene that is not up- and down-regulated in prostate cancer.

- 20 In one embodiment a method for screening for a bioactive agent capable of interfering with the binding of a prostate cancer modulating protein (prostate cancer modulatory protein) or a fragment thereof and an antibody which binds to said prostate cancer modulatory protein or fragment thereof. In a preferred embodiment, the method comprises combining a prostate cancer modulatory protein or fragment thereof, a candidate bioactive agent and an antibody which binds to said prostate cancer modulatory protein or fragment thereof. The method further includes determining the binding of said prostate cancer modulatory protein or fragment thereof and said antibody. Wherein there is a change in binding, an agent is
25 identified as an interfering agent. The interfering agent can be an agonist or an antagonist. Preferably, the agent inhibits prostate cancer.

- Also provided herein are methods of eliciting an immune response in an individual. In one embodiment a method provided herein comprises administering to an individual a composition comprising a prostate cancer modulating protein, or a fragment thereof. In
30 another embodiment, the protein is encoded by a nucleic acid selected from those of Tables 1A-4.

Further provided herein are compositions capable of eliciting an immune response in an individual. In one embodiment, a composition provided herein comprises a prostate cancer modulating protein, preferably encoded by a nucleic acid of Tables 1A-4, or a fragment thereof, and a pharmaceutically acceptable carrier. In another embodiment, said composition comprises a nucleic acid comprising a sequence encoding a prostate cancer modulating protein, preferably selected from the nucleic acids of Tables 1A-4 and a pharmaceutically acceptable carrier.

Also provided are methods of neutralizing the effect of a prostate cancer protein, or a fragment thereof, comprising contacting an agent specific for said protein with said protein in an amount sufficient to effect neutralization. In another embodiment, the protein is encoded by a nucleic acid selected from those of Tables 1A-4. In another aspect of the invention, a method of treating an individual for prostate cancer is provided. In one embodiment, the method comprises administering to said individual an inhibitor of a prostate cancer modulating protein. In another embodiment, the method comprises administering to a patient having prostate cancer an antibody to a prostate cancer modulating protein conjugated to a therapeutic moiety. Such a therapeutic moiety can be a cytotoxic agent or a radioisotope.

DETAILED DESCRIPTION OF THE INVENTION

In accordance with the objects outlined above, the present invention provides novel methods for diagnosis and evaluation of androgen-dependent prostate cells (malignant or non-malignant), prostate cells undergoing androgen withdrawal, and androgen-independent prostate cancer, as well as methods for treating androgen-dependent prostate cells (malignant or non-malignant), prostate cancer undergoing androgen withdrawal, and androgen-independent prostate cancer. The current Specification incorporates the text of USSN 09/976,858, filed October 12, 2001, USSN 60/295,917, filed June 4, 2001, USSN 60/368,689, filed March 29, 2002; USSN 60/350,666, filed November 13, 2001; and USSN 60/372,246, filed April 12, 2002.

Table 1A provides unigene cluster identification numbers for the nucleotide sequence of genes that exhibit increased or decreased expression in androgen-independent prostate cancer samples. Table 1A also provides an exemplar accession number that provides a nucleotide sequence that is part of the unigene cluster. The expression patterns of the genes of Table 1A can be broadly defined into the following categories:

Genes that are expressed early in the time course, then drop off in expression, and then express again with emergence of androgen-independence (hi-lo-hi pattern in table 1A). Genes that are expressed early in the time course, then drop off in expression, and do not express again with emergence of androgen-independence (hi-lo-lo pattern in 1A). Genes that are not expressed early in the time course, but express only with emergence of androgen-independence (lo-lo-hi pattern in table 1A). Genes that are not expressed early in the time course, but then express as androgen is withdrawn and continue to express with emergence of androgen-independence (lo-hi-hi pattern in table 1A). Genes that are not expressed early in the time course, but then express as androgen is withdrawn and drop off again with emergence of androgen-independence (lo-hi-lo pattern in table 1A).

Tables 2A-C provide unigene cluster identification numbers for the nucleotide sequence of genes that exhibit increased or decreased expression in androgen-dependent prostate cancer, prostate cancer undergoing androgen withdrawal and androgen-independent prostate cancer. Tables 2A-C also provide an exemplar accession number that provides a nucleotide sequence that is part of the unigene cluster. The expression patterns of the genes of Tables 2A-C can be broadly defined into the following 6 categories:

Genes that are expressed early in the time course of androgen withdrawal, then drop off in expression, and then express again with emergence of androgen-independence (hi-lo-hi pattern in Table 2A). Genes that are expressed early in the time course, then drop off in expression immediately after androgen-withdrawal, and do not express again with emergence of androgen-independence (hi-lo-lo-lo pattern in Table 2A). Genes that are expressed early in the time course, then drop off in expression after several days of androgen withdrawal, and do not express again with emergence of androgen-independence (hi-hi-lo-lo pattern in Table 2A). Genes that are not expressed early in the time course, but express only with emergence of androgen-independence (lo-lo-lo-hi pattern in Table 2A). Genes that are not expressed early in the time course, but then express as androgen is withdrawn and continue to express with emergence of androgen-independence (lo-lo-hi-hi pattern in Table 2A). Genes that are not expressed early in the time course, but then express as androgen is withdrawn and drop off again with emergence of androgen-independence (lo-lo-hi-lo pattern in Table 2A).

Definitions

The term "androgen ablation therapy" refers to techniques for the removal or destruction of sources of male hormones, such as testosterone. These techniques include, for example, 1) surgical removal of the testicles, 2) medications such as gonadotropin releasing hormone analogs that inhibit testosterone production, or 3) anti-androgenic drugs that block androgen receptors.

The term "androgen-independent prostate cancer protein" or "androgen-independent prostate cancer polynucleotide" or "androgen-independent prostate cancer-associated transcript" refers to nucleic acid and polypeptide polymorphic variants, alleles, mutants, and interspecies homologues that: (1) have a nucleotide sequence that has greater than about 60% nucleotide sequence identity, 65%, 70%, 75%, 80%, 85%, 90%, preferably 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% or greater nucleotide sequence identity, preferably over a region of over a region of at least about 25, 50, 100, 200, 500, 1000, or more nucleotides, to a nucleotide sequence of or associated with a unigene cluster of Tables 1A-4; (2) bind to antibodies, e.g., polyclonal antibodies, raised against an immunogen comprising an amino acid sequence encoded by a nucleotide sequence of or associated with a unigene cluster of Tables 1A-4 and conservatively modified variants thereof; (3) specifically hybridize under stringent hybridization conditions to a nucleic acid sequence, or the complement thereof of Tables 1A-4 and conservatively modified variants thereof; or (4) have an amino acid sequence that has greater than about 60% amino acid sequence identity, 65%, 70%, 75%, 80%, 85%, 90%, preferably 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% or greater amino sequence identity, preferably over a region of over a region of at least about 25, 50, 100, 200, 500, 1000, or more amino acid, to an amino acid sequence encoded by a nucleotide sequence of or associated with a unigene cluster of Tables 1A-4. These polynucleotides or proteins may also be expressed during a period following androgen withdrawal. A polynucleotide or polypeptide sequence is typically from a mammal including, but not limited to, primate, e.g., human; rodent, e.g., rat, mouse, hamster; cow, pig, horse, sheep, or other mammal. A "prostate cancer polypeptide" and a "prostate cancer polynucleotide," include both naturally occurring or recombinant forms, and may refer to those polypeptides or polynucleotides which are expressed in prostate proliferative cells.

A "full length" prostate cancer protein or nucleic acid refers to a prostate cancer polypeptide or polynucleotide sequence, or a variant thereof, that contains the elements normally contained in one or more naturally occurring, wild type prostate cancer

polynucleotide or polypeptide sequences. The “full length” may be prior to, or after, various stages of post-translation processing or splicing, including alternative splicing.

“Biological sample” as used herein is a sample of biological tissue or fluid that contains nucleic acids or polypeptides, e.g., of a prostate cancer protein, polynucleotide or transcript. Such samples include, but are not limited to, tissue isolated from primates, e.g., humans, or rodents, e.g., mice, and rats. Biological samples may also include sections of tissues such as biopsy and autopsy samples, frozen sections taken for histology purposes, blood, plasma, serum, sputum, stool, tears, mucus, hair, skin, etc. Biological samples also include explants and primary and/or transformed cell cultures derived from patient tissues. A biological sample is typically obtained from a eukaryotic organism, most preferably a mammal such as a primate e.g., chimpanzee or human; cow; dog; cat; a rodent, e.g., guinea pig, rat, mouse; rabbit; or a bird; reptile; or fish.

“Providing a biological sample” means to obtain a biological sample for use in methods described in this invention. Most often, this will be done by removing a sample of cells from an animal, but can also be accomplished by using previously isolated cells (e.g., isolated by another person, at another time, and/or for another purpose), by collecting a sample which contains a soluble polypeptide or nucleic acid derived from a prostate cell, or by performing the methods of the invention in vivo. Archival tissues, having treatment or outcome history, will be particularly useful.

The terms “identical” or percent “identity,” in the context of two or more nucleic acids or polypeptide sequences, refer to two or more sequences or subsequences that are the same or have a specified percentage of amino acid residues or nucleotides that are the same (i.e., about 60% identity, preferably 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or higher identity over a specified region, when compared and aligned for maximum correspondence over a comparison window or designated region) as measured using a BLAST or BLAST 2.0 sequence comparison algorithms with default parameters described below, or by manual alignment and visual inspection (see, e.g., NCBI web site <http://www.ncbi.nlm.nih.gov/BLAST/> or the like). Such sequences are then said to be “substantially identical.” This definition also refers to, or may be applied to, the complement of a test sequence. The definition also includes sequences that have deletions and/or additions, as well as those that have substitutions, as well as naturally occurring, e.g., polymorphic or allelic variants, and man-made variants. As described below, the preferred

algorithms can account for gaps and the like. Preferably, identity exists over a region that is at least about 25 amino acids or nucleotides in length, or more preferably over a region that is 50-100 amino acids or nucleotides in length.

For sequence comparison, typically one sequence acts as a reference sequence, to which test sequences are compared. When using a sequence comparison algorithm, test and reference sequences are entered into a computer, subsequence coordinates are designated, if necessary, and sequence algorithm program parameters are designated. Preferably, default program parameters can be used, or alternative parameters can be designated. The sequence comparison algorithm then calculates the percent sequence identities for the test sequences relative to the reference sequence, based on the program parameters.

A "comparison window", as used herein, includes reference to a segment of one of the number of contiguous positions selected from the group consisting typically of from 20 to 600, usually about 50 to about 200, more usually about 100 to about 150 in which a sequence may be compared to a reference sequence of the same number of contiguous positions after the two sequences are optimally aligned. Methods of alignment of sequences for comparison are well-known in the art. Optimal alignment of sequences for comparison can be conducted, e.g., by the local homology algorithm of Smith and Waterman (1981) Appl. Math. 2:482, by the homology alignment algorithm of Needleman and Wunsch (1970) J. Mol. Biol. 48:443-453, by the search for similarity method of Pearson and Lipman (1988) Proc. Nat'l. Acad. Sci. USA 85:2444-2448, by computerized implementations of these algorithms (GAP, BESTFIT, FASTA, and TFASTA in the Wisconsin Genetics Software Package, Genetics Computer Group, 575 Science Dr., Madison, WI), or by manual alignment and visual inspection (see, e.g., Ausubel, et al. (eds. 1995 and supplements) Current Protocols in Molecular Biology Lippincott).

Preferred examples of algorithms that are suitable for determining percent sequence identity and sequence similarity include the BLAST and BLAST 2.0 algorithms, which are described in Altschul, et al. (1977) Nuc. Acids Res. 25:3389-3402 and Altschul, et al. (1990) J. Mol. Biol. 215:403-410. BLAST and BLAST 2.0 are used, with the parameters described herein, to determine percent sequence identity for the nucleic acids and proteins of the invention. Software for performing BLAST analyses is publicly available through the National Center for Biotechnology Information (<http://www.ncbi.nlm.nih.gov/>). This algorithm involves first identifying high scoring sequence pairs (HSPs) by identifying short

words of length W in the query sequence, which either match or satisfy some positive-valued threshold score T when aligned with a word of the same length in a database sequence. T is referred to as the neighborhood word score threshold (Altschul, et al., supra). These initial neighborhood word hits act as seeds for initiating searches to find longer HSPs containing them. The word hits are extended in both directions along each sequence for as far as the cumulative alignment score can be increased. Cumulative scores are calculated using, e.g., for nucleotide sequences, the parameters M (reward score for a pair of matching residues; always > 0) and N (penalty score for mismatching residues; always < 0). For amino acid sequences, a scoring matrix is used to calculate the cumulative score. Extension of the word hits in each direction are halted when: the cumulative alignment score falls off by the quantity X from its maximum achieved value; the cumulative score goes to zero or below, due to the accumulation of one or more negative-scoring residue alignments; or the end of either sequence is reached. The BLAST algorithm parameters W, T, and X determine the sensitivity and speed of the alignment. The BLASTN program (for nucleotide sequences) uses as defaults a wordlength (W) of 11, an expectation (E) of 10, M=5, N=-4 and a comparison of both strands. For amino acid sequences, the BLASTP program uses as defaults a wordlength of 3, and expectation (E) of 10, and the BLOSUM62 scoring matrix (see Henikoff and Henikoff (1989) Proc. Natl. Acad. Sci. USA 89:10915-919) alignments (B) of 50, expectation (E) of 10, M=5, N=-4, and a comparison of both strands.

The BLAST algorithm also performs a statistical analysis of the similarity between two sequences (see, e.g., Karlin and Altschul (1993) Proc. Nat'l. Acad. Sci. USA 90:5873-5787). One measure of similarity provided by the BLAST algorithm is the smallest sum probability (P(N)), which provides an indication of the probability by which a match between two nucleotide or amino acid sequences would occur by chance. For example, a nucleic acid is considered similar to a reference sequence if the smallest sum probability in a comparison of the test nucleic acid to the reference nucleic acid is less than about 0.2, more preferably less than about 0.01, and most preferably less than about 0.001. Log values may be large negative numbers, e.g., 5, 10, 20, 30, 40, 40, 70, 90, 110, 150, 170, etc.

An indication that two nucleic acid sequences or polypeptides are substantially identical is that the polypeptide encoded by the first nucleic acid is immunologically cross reactive with the antibodies raised against the polypeptide encoded by the second nucleic acid, as described below. Thus, a polypeptide is typically substantially identical to a second

polypeptide, e.g., where the two peptides differ only by conservative substitutions. Another indication that two nucleic acid sequences are substantially identical is that the two molecules or their complements hybridize to each other under stringent conditions, as described below. Yet another indication that two nucleic acid sequences are substantially identical is that the same primers can be used to amplify the sequences.

A "host cell" is a naturally occurring cell or a transformed cell that contains an expression vector and supports the replication or expression of the expression vector. Host cells may be cultured cells, explants, cells in vivo, and the like. Host cells may be prokaryotic cells such as *E. coli*, or eukaryotic cells such as yeast, insect, amphibian, or mammalian cells such as CHO, HeLa, and the like (see, e.g., the American Type Culture Collection catalog or web site, www.atcc.org).

The terms "isolated," "purified," or "biologically pure" refer to material that is substantially or essentially free from components that normally accompany it as found in its native state. Purity and homogeneity are typically determined using analytical chemistry techniques such as polyacrylamide gel electrophoresis or high performance liquid chromatography. A protein or nucleic acid that is the predominant species present in a preparation is substantially purified. In particular, an isolated nucleic acid is separated from some open reading frames that naturally flank the gene and encode proteins other than protein encoded by the gene. The term "purified" in some embodiments denotes that a nucleic acid or protein gives rise to essentially one band in an electrophoretic gel. Preferably, it means that the nucleic acid or protein is at least 85% pure, more preferably at least 95% pure, and most preferably at least 99% pure. "Purify" or "purification" in other embodiments means removing at least one contaminant from the composition to be purified. In this sense, purification does not require that the purified compound be homogenous, e.g., 100% pure.

The terms "polypeptide," "peptide," and "protein" are used interchangeably herein to refer to a polymer of amino acid residues. The terms apply to amino acid polymers in which one or more amino acid residue is an artificial chemical mimetic of a corresponding naturally occurring amino acid, as well as to naturally occurring amino acid polymers, those containing modified residues, and non-naturally occurring amino acid polymer. Certain diagnostic methods may evaluate secreted or breakdown products present only because the producing cell is present, and would otherwise be absent in a normal individual.

The term "amino acid" refers to naturally occurring and synthetic amino acids, as well as amino acid analogs and amino acid mimetics that function similarly to the naturally occurring amino acids. Naturally occurring amino acids are those encoded by the genetic code, as well as those amino acids that are later modified, e.g., hydroxyproline, γ -carboxyglutamate, and O-phosphoserine. Amino acid analogs refers to compounds that have the same basic chemical structure as a naturally occurring amino acid, e.g., an α carbon that is bound to a hydrogen, a carboxyl group, an amino group, and an R group, e.g., homoserine, norleucine, methionine sulfoxide, methionine methyl sulfonium. Such analogs may have modified R groups (e.g., norleucine) or modified peptide backbones, but retain the same basic chemical structure as a naturally occurring amino acid. Amino acid mimetics refers to chemical compounds that have a structure that is different from the general chemical structure of an amino acid, but that functions similarly to a naturally occurring amino acid.

Amino acids may be referred to herein by either their commonly known three letter symbols or by the one-letter symbols recommended by the IUPAC-IUB Biochemical Nomenclature Commission. Nucleotides, likewise, may be referred to by their commonly accepted single-letter codes.

"Conservatively modified variants" applies to both amino acid and nucleic acid sequences. With respect to particular nucleic acid sequences, conservatively modified variants refers to those nucleic acids which encode identical or essentially identical amino acid sequences, or where the nucleic acid does not encode an amino acid sequence, to essentially identical or associated, e.g., naturally contiguous, sequences. Because of the degeneracy of the genetic code, a large number of functionally identical nucleic acids encode most proteins. For instance, the codons GCA, GCC, GCG, and GCU encode the amino acid alanine. Thus, at every position where an alanine is specified by a codon, the codon can be altered to another of the corresponding codons described without altering the encoded polypeptide. Such nucleic acid variations are "silent variations," which are one species of conservatively modified variations. Every nucleic acid sequence herein which encodes a polypeptide also describes silent variations of the nucleic acid. One of skill will recognize that in certain contexts each codon in a nucleic acid (except AUG, which is ordinarily the only codon for methionine, and TGG, which is ordinarily the only codon for tryptophan) can be modified to yield a functionally identical molecule. Accordingly, often silent variations of

a nucleic acid which encodes a polypeptide is implicit in a described sequence with respect to the expression product, but not with respect to actual probe sequences.

As to amino acid sequences, one of skill will recognize that individual substitutions, deletions or additions to a nucleic acid, peptide, polypeptide, or protein sequence which alters, adds or deletes a single amino acid or a small percentage of amino acids in the encoded sequence is a "conservatively modified variant" where the alteration results in the substitution of an amino acid with a chemically similar amino acid. Conservative substitutions providing functionally similar amino acids are well known in the art. Such conservatively modified variants are in addition to and do not exclude polymorphic variants, interspecies homologs, and alleles of the invention, typically conservative substitutions for one another: 1) Alanine (A), Glycine (G); 2) Aspartic acid (D), Glutamic acid (E); 3) Asparagine (N), Glutamine (Q); 4) Arginine (R), Lysine (K); 5) Isoleucine (I), Leucine (L), Methionine (M), Valine (V); 6) Phenylalanine (F), Tyrosine (Y), Tryptophan (W); 7) Serine (S), Threonine (T); and 8) Cysteine (C), Methionine (M) (see, e.g., Creighton (1984) Proteins Freeman).

Macromolecular structures such as polypeptide structures can be described in terms of various levels of organization. For a general discussion of this organization, see, e.g., Alberts, et al. (2001) Molecular Biology of the Cell (4th ed.) and Cantor and Schimmel (1980) Biophysical Chemistry Part I: The Conformation of Biological Macromolecules Freeman. "Primary structure" refers to the amino acid sequence of a particular peptide. "Secondary structure" refers to locally ordered, three dimensional structures within a polypeptide. These structures are commonly known as domains. Domains are portions of a polypeptide that often form a compact unit of the polypeptide and are typically 25 to approximately 500 amino acids long. Typical domains are made up of sections of lesser organization such as stretches of β -sheet and α -helices. "Tertiary structure" refers to the complete three dimensional structure of a polypeptide monomer. "Quaternary structure" refers to the three dimensional structure formed, usually by the noncovalent association of independent tertiary units. Anisotropic terms are also known as energy terms.

"Nucleic acid" or "oligonucleotide" or "polynucleotide" or grammatical equivalents used herein means at least two nucleotides covalently linked together. Oligonucleotides are typically from about 5, 6, 7, 8, 9, 10, 12, 15, 25, 30, 40, 50 or more nucleotides in length, up to about 100 nucleotides in length. Nucleic acids and polynucleotides are a polymers of virtually any length, including longer lengths, e.g., 200, 300, 500, 1000, 2000, 3000, 5000,

7000, 10,000, etc. A nucleic acid of the present invention will generally contain phosphodiester bonds, although in some cases, nucleic acid analogs are included that may have alternate backbones, comprising, e.g., phosphoramidate, phosphorothioate, phosphorodithioate, or O-methylphosphoroamidite linkages (see Eckstein (1992)

- 5 Oligonucleotides and Analogues: A Practical Approach, Oxford University Press); and peptide nucleic acid backbones and linkages. Other analog nucleic acids include those with positive backbones; non-ionic backbones, and non-ribose backbones, including those described in U.S. Patent Nos. 5,235,033 and 5,034,506, and Chapters 6 and 7, ASC Symposium Series 580, Sanghvi and Cook (eds. 1994) Carbohydrate Modifications in
10 Antisense Research ACS Symposium Series 580. Nucleic acids containing one or more carbocyclic sugars are also included within one definition of nucleic acids. Modifications of the ribose-phosphate backbone may be done for a variety of reasons, e.g., to increase the stability and half-life of such molecules in physiological environments or as probes on a biochip. Mixtures of naturally occurring nucleic acids and analogs can be made;
15 alternatively, mixtures of different nucleic acid analogs, and mixtures of naturally occurring nucleic acids and analogs may be made.

A variety of references disclose such nucleic acid analogs, including, for example, phosphoramidate (Beaucage, et al. (1993) Tetrahedron 49(10):1925-1963 and references therein; Letsinger (1970) J. Org. Chem. 35:3800-3803; Sprinzl, et al. (1977) Eur. J. Biochem.
20 81:579-589; Letsinger, et al. (1986) Nucl. Acids Res. 14:3487-499; Sawai, et al. (1984) Chem. Lett. 805; Letsinger, et al. (1988) J. Am. Chem. Soc. 110:4470-4471; and Pauwels, et al. (1986) Chemica Scripta 26:141-149), phosphorothioate (Mag, et al. (1991) Nucleic Acids Res. 19:1437-441; and U.S. Patent No. 5,644,048), phosphorodithioate (Briu, et al. (1989) J. Am. Chem. Soc. 111:2321-xxx, O-methylphosphoroamidite linkages (see Eckstein (1992)
25 Oligonucleotides and Analogues: A Practical Approach Oxford University Press), and peptide nucleic acid backbones and linkages (see Egholm (1992) J. Am. Chem. Soc. 114:1895-1897; Meier, et al. (1992) Chem. Int. Ed. Engl. 31:1008-1010; Nielsen (1993) Nature 365:566-568; Carlsson, et al. (1996) Nature 380:207, each of which is incorporated by reference). Other analog nucleic acids include those with positive backbones (Denpoy, et al.
30 (1995) Proc. Natl. Acad. Sci. USA 92:6097-101; non-ionic backbones (U.S. Patent Nos. 5,386,023, 5,637,684, 5,602,240, 5,216,141 and 4,469,863; Kiedrowshi, et al. (1991) Angew. Chem. Intl. Ed. English 30:423-426; Letsinger, et al. (1988) J. Am. Chem. Soc. 110:4470;

Letsinger, et al. (1994) Nucleoside and Nucleotide 13:1597-xxx; Chapters 2 and 3 in Sanghvi and Cook (eds. 1994) Carbohydrate Modifications in Antisense Research ACS Symposium Series 580; Mesmaeker, et al. (1994) Bioorganic and Medicinal Chem. Lett. 4:395-xxx; Jeffs, et al. (1994) J. Biomolecular NMR 34:17; Horn (1996) Tetrahedron Lett. 37:743-xxx) and non-ribose backbones, including those described in U.S. Patent Nos. 5,235,033 and 5,034,506, and Chapters 6 and 7 in Sanghvi and Cook (eds. 1994) Carbohydrate Modifications in Antisense Research ACS Symposium Series 580. Nucleic acids containing one or more carbocyclic sugars are also included within one definition of nucleic acids (see Jenkins, et al. (1995) Chem. Soc. Rev. xx:169-176). Several nucleic acid analogs are described in Rawls (p. 35, June 2, 1997) C&E News. Each of these references is hereby expressly incorporated by reference.

Particularly preferred are peptide nucleic acids (PNA) which includes peptide nucleic acid analogs. These backbones are substantially non-ionic under neutral conditions, in contrast to the highly charged phosphodiester backbone of naturally occurring nucleic acids. This results in two advantages. First, the PNA backbone exhibits improved hybridization kinetics. PNAs have larger changes in the melting temperature (T_m) for mismatched versus perfectly matched base pairs. DNA and RNA typically exhibit a 2-4° C drop in T_m for an internal mismatch. With the non-ionic PNA backbone, the drop is closer to 7-9° C. Similarly, due to their non-ionic nature, hybridization of the bases attached to these backbones is relatively insensitive to salt concentration. In addition, PNAs are not degraded by cellular enzymes, and thus can be more stable.

The nucleic acids may be single stranded or double stranded, as specified, or contain portions of both double stranded or single stranded sequence. As will be appreciated by those in the art, the depiction of a single strand also defines the sequence of the complementary strand; thus the sequences described herein also provide the complement of the sequence. The nucleic acid may be DNA, both genomic and cDNA, RNA or a hybrid, where the nucleic acid may contain combinations of deoxyribo- and ribo-nucleotides, and combinations of bases, including uracil, adenine, thymine, cytosine, guanine, inosine, xanthine hypoxanthine, isocytosine, isoguanine, etc. "Transcript" typically refers to a naturally occurring RNA, e.g., a pre-mRNA, hnRNA, or mRNA. As used herein, the term "nucleoside" includes nucleotides and nucleoside and nucleotide analogs, and modified nucleosides such as amino modified nucleosides. In addition, "nucleoside" includes non-naturally occurring analog structures.

Thus, e.g., the individual units of a peptide nucleic acid, each containing a base, are referred to herein as a nucleoside.

A "label" or a "detectable moiety" is a composition detectable by spectroscopic, photochemical, biochemical, immunochemical, chemical, or other physical means. For example, useful labels include ³²P, fluorescent dyes, electron-dense reagents, enzymes (e.g., as commonly used in an ELISA), biotin, digoxigenin, or haptens and proteins or other entities which can be made detectable, e.g., by incorporating a radiolabel into the peptide or used to detect antibodies specifically reactive with the peptide. The labels may be incorporated into the prostate cancer nucleic acids, proteins, and antibodies at virtually any position. Many methods for conjugating the antibody to the label may be employed, including those methods described by Hunter, et al. (1962) Nature, 144:945; David, et al. (1974) Biochemistry 13:1014-1021; Pain, et al. (1981) J. Immunol. Meth. 40:219-230; and Nygren (1982) J. Histochem. and Cytochem. 30:407-412.

An "effector" or "effector moiety" or "effector component" is a molecule that is bound (or linked, or conjugated), either covalently, through a linker or a chemical bond, or noncovalently, through ionic, van der Waals, electrostatic, or hydrogen bonds, to an antibody. The "effector" can be a variety of molecules including, e.g., detection moieties including radioactive compounds, fluorescent compounds, an enzyme or substrate, tags such as epitope tags, a toxin; activatable moieties, a chemotherapeutic agent; a lipase; an antibiotic; or a radioisotope emitting "hard" e.g., beta radiation.

A "labeled nucleic acid probe or oligonucleotide" is one that is bound, either covalently, through a linker or a chemical bond, or noncovalently, through ionic, van der Waals, electrostatic, or hydrogen bonds to a label such that the presence of the probe may be detected by detecting the presence of the label bound to the probe. Alternatively, method using high affinity interactions may achieve the same results where one of a pair of binding partners binds to the other, e.g., biotin, streptavidin.

As used herein a "nucleic acid probe or oligonucleotide" is defined as a nucleic acid capable of binding to a target nucleic acid of complementary sequence through one or more types of chemical bonds, usually through complementary base pairing, usually through hydrogen bond formation. As used herein, a probe may include natural (i.e., A, G, C, or T) or modified bases (7-deazaguanosine, inosine, etc.). In addition, the bases in a probe may be joined by a linkage other than a phosphodiester bond, so long as it does not functionally

interfere with hybridization. Thus, e.g., probes may be peptide nucleic acids in which the constituent bases are joined by peptide bonds rather than phosphodiester linkages. It will be understood by one of skill in the art that probes may bind target sequences lacking complete complementarity with the probe sequence depending upon the stringency of the hybridization conditions. The probes are preferably directly labeled as with isotopes, chromophores, lumiphores, chromogens, or indirectly labeled such as with biotin to which a streptavidin complex may later bind. By assaying for the presence or absence of the probe, one can detect the presence or absence of the select sequence or subsequence. Diagnosis or prognosis may be based at the genomic level, or at the level of RNA or protein expression.

The term "recombinant" when used with reference, e.g., to a cell, or nucleic acid, protein, or vector, indicates that the cell, nucleic acid, protein or vector, has been modified by the introduction of a heterologous nucleic acid or protein or the alteration of a native nucleic acid or protein, or that the cell is derived from a cell so modified. Thus, e.g., recombinant cells express genes that are not found within the native (non-recombinant) form of the cell or express native genes that are otherwise abnormally expressed, under expressed or not expressed at all. By the term "recombinant nucleic acid" herein is meant nucleic acid, originally formed in vitro, in general, by the manipulation of nucleic acid, e.g., using polymerases and endonucleases, in a form not normally found in nature. In this manner, operably linkage of different sequences is achieved. Thus an isolated nucleic acid, in a linear form, or an expression vector formed in vitro by ligating DNA molecules that are not normally joined, are both considered recombinant for the purposes of this invention. It is understood that once a recombinant nucleic acid is made and reintroduced into a host cell or organism, it will replicate non-recombinantly, i.e., using the in vivo cellular machinery of the host cell rather than in vitro manipulations; however, such nucleic acids, once produced recombinantly, although subsequently replicated non-recombinantly, are still considered recombinant for the purposes of the invention. Similarly, a "recombinant protein" is a protein made using recombinant techniques, i.e., through the expression of a recombinant nucleic acid as depicted above.

The term "heterologous" when used with reference to portions of a nucleic acid indicates that the nucleic acid comprises two or more subsequences that are not normally found in the same relationship to each other in nature. For instance, the nucleic acid is typically recombinantly produced, having two or more sequences, e.g., from unrelated genes

arranged to make a new functional nucleic acid, e.g., a promoter from one source and a coding region from another source. Similarly, a heterologous protein will often refer to two or more subsequences that are not found in the same relationship to each other in nature (e.g., a fusion protein).

5 A "promoter" is defined as an array of nucleic acid control sequences that direct transcription of a nucleic acid. As used herein, a promoter includes necessary nucleic acid sequences near the start site of transcription, such as, in the case of a polymerase II type promoter, a TATA element. A promoter also optionally includes distal enhancer or repressor elements, which can be located as much as several thousand base pairs from the start site of
10 transcription. A "constitutive" promoter is a promoter that is active under most environmental and developmental conditions. An "inducible" promoter is a promoter that is active under environmental or developmental regulation. The term "operably linked" refers to a functional linkage between a nucleic acid expression control sequence (such as a promoter, or array of transcription factor binding sites) and a second nucleic acid sequence,
15 wherein the expression control sequence directs transcription of the nucleic acid corresponding to the second sequence.

An "expression vector" is a nucleic acid construct, generated recombinantly or synthetically, with a series of specified nucleic acid elements that permit transcription of a particular nucleic acid in a host cell. The expression vector can be part of a plasmid, virus, or
20 nucleic acid fragment. Typically, the expression vector includes a nucleic acid to be transcribed operably linked to a promoter.

The phrase "selectively (or specifically) hybridizes to" refers to the binding, duplexing, or hybridizing of a molecule only to a particular nucleotide sequence under stringent hybridization conditions when that sequence is present in a complex mixture (e.g.,
25 total cellular or library DNA or RNA).

The phrase "stringent hybridization conditions" refers to conditions under which a probe will hybridize to its target subsequence, typically in a complex mixture of nucleic acids, but to no other sequences. Stringent conditions are sequence-dependent and will be different in different circumstances. Longer sequences hybridize specifically at higher
30 temperatures. An extensive guide to the hybridization of nucleic acids is found "Overview of principles of hybridization and the strategy of nucleic acid assays" in Tijssen (1993) Hybridization with Nucleic Probes (Techniques in Biochemistry and Molecular Biology vol.

24) Elsevier. Generally, stringent conditions are selected to be about 5-10° C lower than the thermal melting point (T_m) for the specific sequence at a defined ionic strength pH. The T_m is the temperature (under defined ionic strength, pH, and nucleic concentration) at which 50% of the probes complementary to the target hybridize to the target sequence at equilibrium (as the target sequences are present in excess, at T_m , 50% of the probes are occupied at equilibrium). Stringent conditions will be those in which the salt concentration is less than about 1.0 M sodium ion, typically about 0.01 to 1.0 M sodium ion concentration (or other salts) at pH 7.0 to 8.3 and the temperature is at least about 30° C for short probes (e.g., 10 to 50 nucleotides) and at least about 60° C for long probes (e.g., greater than 50 nucleotides). Stringent conditions may also be achieved with the addition of destabilizing agents such as formamide. For selective or specific hybridization, a positive signal is at least two times background, preferably 10 times background hybridization. Exemplary stringent hybridization conditions can be as following: 50% formamide, 5x SSC, and 1% SDS, incubating at 42° C, or, 5x SSC, 1% SDS, incubating at 65° C, with wash in 0.2x SSC, and 0.1% SDS at 65° C. For PCR, a temperature of about 36° C is typical for low stringency amplification, although annealing temperatures may vary between about 32° C and 48° C depending on primer length. For high stringency PCR amplification, a temperature of about 62° C is typical, although high stringency annealing temperatures can range from about 50-65° C, depending on the primer length and specificity. Typical cycle conditions for both high and low stringency amplifications include a denaturation phase of 90-95° C for 30-120 sec, an annealing phase lasting 30-120 sec, and an extension phase of about 72° C for 1-2 min. Protocols and guidelines for low and high stringency amplification reactions are provided, e.g., in Innis, et al. (1990) PCR Protocols: A Guide to Methods and Applications Academic Press, N.Y.

Nucleic acids that do not hybridize to each other under stringent conditions are still substantially identical if the polypeptides which they encode are substantially identical. This occurs, e.g., when a copy of a nucleic acid is created using the maximum codon degeneracy permitted by the genetic code. In such cases, the nucleic acids typically hybridize under moderately stringent hybridization conditions. Exemplary "moderately stringent hybridization conditions" include a hybridization in a buffer of 40% formamide, 1 M NaCl, 1% SDS at 37° C, and a wash in 1X SSC at 45° C. A positive hybridization is at least twice

background. Those of ordinary skill will readily recognize that alternative hybridization and wash conditions can be utilized to provide conditions of similar stringency. Additional guidelines for determining hybridization parameters are provided in numerous references, e.g., Ausubel, et al. (eds. 1991 and supplements) Current Protocols in Molecular Biology

5 The phrase “functional effects” in the context of assays for testing compounds that modulate activity of a prostate cancer protein includes the determination of a parameter that is indirectly or directly under the influence of the prostate cancer protein or nucleic acid, e.g., a functional, physical, or chemical effect, such as the ability to decrease prostate proliferation (malignant or non-malignant). It includes ligand binding activity; cell growth on soft agar;
10 anchorage dependence; contact inhibition and density limitation of growth; cellular proliferation; cellular transformation; growth factor or serum dependence; tumor specific marker levels; invasiveness into Matrigel; tumor growth and metastasis in vivo; mRNA and protein expression in cells undergoing metastasis, and other characteristics of prostate cancer cells. “Functional effects” include in vitro, in vivo, and ex vivo activities.

15 By “determining the functional effect” is meant assaying for a compound that increases or decreases a parameter that is indirectly or directly under the influence of a prostate cancer protein sequence, e.g., functional, enzymatic, physical and chemical effects. Such functional effects can be measured by means known to those skilled in the art, e.g., changes in spectroscopic characteristics (e.g., fluorescence, absorbance, refractive index),
20 hydrodynamic (e.g., shape), chromatographic, or solubility properties for the protein, measuring inducible markers or transcriptional activation of the prostate cancer protein; measuring binding activity or binding assays, e.g., binding to antibodies or other ligands, and measuring cellular proliferation. Determination of the functional effect of a compound on prostate cancer can also be performed using prostate cancer assays known to those of skill in
25 the art such as an in vitro assays, e.g., cell growth on soft agar; anchorage dependence; contact inhibition and density limitation of growth; cellular proliferation; cellular transformation; growth factor or serum dependence; tumor specific marker levels; invasiveness into Matrigel; tumor growth and metastasis in vivo; mRNA and protein expression in cells undergoing metastasis, and other characteristics of prostate cancer cells.
30 The functional effects can be evaluated by many means known to those skilled in the art, e.g., microscopy for quantitative or qualitative measures of alterations in morphological features, measurement of changes in RNA or protein levels for prostate cancer-associated sequences,

measurement of RNA stability, identification of downstream or reporter gene expression (CAT, luciferase, β -gal, GFP, and the like), e.g., via chemiluminescence, fluorescence, colorimetric reactions, antibody binding, inducible markers, and ligand binding assays.

“Inhibitors”, “activators”, and “modulators” of prostate cancer polynucleotide and polypeptide sequences are used to refer to activating, inhibitory, or modulating molecules or compounds identified using *in vitro* and *in vivo* assays of prostate cancer polynucleotide and polypeptide sequences. Inhibitors are compounds that, e.g., bind to, partially or totally block activity, decrease, prevent, delay activation, inactivate, desensitize, or down regulate the activity or expression of prostate cancer proteins, e.g., antagonists. Antisense nucleic acids may seem to inhibit expression and subsequent function of the protein. “Activators” are compounds that increase, open, activate, facilitate, enhance activation, sensitize, agonize, or up regulate prostate cancer protein activity. Inhibitors, activators, or modulators also include genetically modified versions of prostate cancer proteins, e.g., versions with altered activity, as well as naturally occurring and synthetic ligands, antagonists, agonists, antibodies, small chemical molecules and the like. Such assays for inhibitors and activators include, e.g., expressing the prostate cancer protein *in vitro*, in cells, or cell membranes, applying putative modulator compounds, and then determining the functional effects on activity, as described above. Activators and inhibitors of prostate cancer can also be identified by incubating prostate cancer cells with the test compound and determining increases or decreases in the expression of 1 or more prostate cancer proteins, e.g., 1, 2, 3, 4, 5, 10, 15, 20, 25, 30, 40, 50 or more prostate cancer proteins, such as prostate cancer proteins encoded by the sequences set out in Tables 1A-4.

Samples or assays comprising prostate cancer proteins that are treated with a potential activator, inhibitor, or modulator are compared to control samples without the inhibitor, activator, or modulator to examine the extent of inhibition. Control samples (untreated with inhibitors) are assigned a relative protein activity value of 100%. Inhibition of a polypeptide is achieved when the activity value relative to the control is about 80%, preferably 50%, more preferably 25-0%. Activation of a prostate cancer polypeptide is achieved when the activity value relative to the control (untreated with activators) is 110%, more preferably 150%, more preferably 200-500% (i.e., two to five fold higher relative to the control), more preferably 1000-3000% higher.

The phrase “changes in cell growth” refers to a change in cell growth and proliferation characteristics in vitro or in vivo, such as cell viability, formation of foci, anchorage independence, semi-solid or soft agar growth, changes in contact inhibition and density limitation of growth, loss of growth factor or serum requirements, changes in cell morphology, gaining or losing immortalization, gaining or losing tumor specific markers, ability to form or suppress tumors when injected into suitable animal hosts, and/or immortalization of the cell. See, e.g., pp. 231-241 in Freshney (1994) Culture of Animal Cells: A Manual of Basic Technique (3d ed.) Wiley-Liss.

“Tumor cell” refers to precancerous, cancerous, and/or normal cells in a tumor.

“Cancer cells,” “transformed” cells, or “transformation” in tissue culture, refers to spontaneous or induced phenotypic changes that do not necessarily involve the uptake of new genetic material. Although transformation can arise from infection with a transforming virus and incorporation of new genomic DNA, or uptake of exogenous DNA, it can also arise spontaneously or following exposure to a carcinogen, thereby mutating an endogenous gene. Transformation is associated with phenotypic changes, such as immortalization of cells, aberrant growth control, nonmorphological changes, and/or malignancy. See, Freshney (2001) Culture of Animal Cells: A Manual of Basic Technique (4th ed.) Wiley-Liss.

“Antibody” refers to a polypeptide comprising a framework region from an immunoglobulin gene or fragments thereof that specifically binds and recognizes an antigen.

The recognized immunoglobulin genes include the kappa, lambda, alpha, gamma, delta, epsilon, and mu constant region genes, as well as the myriad immunoglobulin variable region genes. Light chains are classified as either kappa or lambda. Heavy chains are classified as gamma, mu, alpha, delta, or epsilon, which in turn define the immunoglobulin classes, IgG, IgM, IgA, IgD, and IgE, respectively. Typically, the antigen-binding region of an antibody or its functional equivalent will be most critical in specificity and affinity of binding. See Paul (ed. 1999) Fundamental Immunology (4th ed.) Raven.

An exemplary immunoglobulin (antibody) structural unit comprises a tetramer. Each tetramer is composed of two identical pairs of polypeptide chains, each pair having one “light” (about 25 kD) and one “heavy” chain (about 50-70 kD). The N-terminus of each chain defines a variable region of about 100 to 110 or more amino acids primarily responsible for antigen recognition. The terms variable light chain (V_L) and variable heavy chain (V_H) refer to these light and heavy chains respectively.

Antibodies exist, e.g., as intact immunoglobulins or as a number of well-characterized fragments produced by digestion with various peptidases. Thus, e.g., pepsin digests an antibody below the disulfide linkages in the hinge region to produce $F(ab)'_2$, a dimer of Fab which itself is a light chain joined to V_H-C_H1 by a disulfide bond. The $F(ab)'_2$ may be reduced under mild conditions to break the disulfide linkage in the hinge region, thereby converting the $F(ab)'_2$ dimer into an Fab' monomer. The Fab' monomer is essentially Fab with part of the hinge region (see Paul (ed. 1993) Fundamental Immunology (3d ed.) Raven. While various antibody fragments are defined in terms of the digestion of an intact antibody, one of skill will appreciate that such fragments may be synthesized de novo either chemically or by using recombinant DNA methodology. Thus, the term antibody, as used herein, also includes antibody fragments either produced by the modification of whole antibodies, or those synthesized de novo using recombinant DNA methodologies (e.g., single chain Fv) or those identified using phage display libraries (see, e.g., McCafferty, et al. (1990) Nature 348:552-554.

For preparation of antibodies, e.g., recombinant, monoclonal, or polyclonal antibodies, many technique known in the art can be used (see, e.g., Kohler and Milstein (1975) Nature 256:495-497; Kozbor, et al. (1983) Immunology Today 4:72; pp. 77-96 in Cole, et al. (1985) Monoclonal Antibodies and Cancer Therapy Liss; Coligan (1991) Current Protocols in Immunology Lippincott; Harlow and Lane (1988) Antibodies: A Laboratory Manual CSH Press; and Goding (1986) Monoclonal Antibodies: Principles and Practice (2d ed.) Academic Press. Techniques for the production of single chain antibodies (U.S. Patent 4,946,778) can be adapted to produce antibodies to polypeptides of this invention. Also, transgenic mice, or other organisms such as other mammals, may be used to express humanized antibodies. Alternatively, phage display technology can be used to identify antibodies and heteromeric Fab fragments that specifically bind to selected antigens (see, e.g., McCafferty, et al. (1990) Nature 348:552-554; Marks, et al. (1992) Biotechnology 10:779-783).

A "chimeric antibody" is an antibody molecule in which (a) the constant region, or a portion thereof, is altered, replaced or exchanged so that the antigen binding site (variable region) is linked to a constant region of a different or altered class, effector function and/or species, or an entirely different molecule which confers new properties to the chimeric antibody, e.g., an enzyme, toxin, hormone, growth factor, drug, etc.; or (b) the variable

region, or a portion thereof, is altered, replaced or exchanged with a variable region having a different or altered antigen specificity.

Identification of prostate cancer-associated sequences

- 5 In one aspect, the expression levels of genes are determined in different patient samples for which diagnosis information is desired, to provide expression profiles. An expression profile of a particular sample is essentially a "fingerprint" of the state of the sample; while two states may have a particular gene similarly expressed, the evaluation of a number of genes simultaneously allows the generation of a gene expression profile that is
- 10 characteristic of the state of the cell. That is, normal tissue (e.g., normal prostate or other tissue) may be distinguished from pathological prostate cells, e.g., cancerous or metastatic cancerous tissue of the prostate, or prostate cancer tissue or metastatic prostate cancerous tissue can be compared with tissue samples of prostate and other tissues from surviving cancer patients. By comparing expression profiles of tissue in known different prostate
- 15 cancer states, information regarding which genes are important (including both up- and down-regulation of genes) in each of these states is obtained.

- The identification of sequences that are differentially expressed in prostate cancer versus non-prostate cancer tissue allows the use of this information in a number of ways. For example, a particular treatment regime may be evaluated: does a chemotherapeutic drug act
- 20 to down-regulate prostate cancer or other proliferative disorders, and thus tumor growth or recurrence, in a particular patient. Alternatively, a treatment step may induce other markers which may be used as targets to destroy tumor cells. Similarly, diagnosis and treatment outcomes may be done or confirmed by comparing patient samples with the known expression profiles. Malignant disease may be compared to non-malignant conditions.
- 25 Metastatic tissue can also be analyzed to determine the stage of prostate cancer in the tissue, or origin of primary tumor, e.g., metastasis from a remote primary site. Furthermore, these gene expression profiles (or individual genes) allow screening of drug candidates with an eye to mimicking or altering a particular expression profile; e.g., screening can be done for drugs that suppress the prostate cancer expression profile. This may be done by making biochips
- 30 comprising sets of the important prostate cancer genes, which can then be used in these screens. These methods can also be done on the protein basis; that is, protein expression levels of the prostate cancer proteins can be evaluated for diagnostic purposes or to screen

candidate agents. In addition, the prostate cancer nucleic acid sequences can be administered for gene therapy purposes, including the administration of antisense nucleic acids, or the prostate cancer proteins (including antibodies and other modulators thereof) administered as therapeutic drugs.

5 Thus the present invention provides nucleic acid and protein sequences that are differentially expressed in prostate cancer relative to normal tissues and/or non-malignant disease, or in different types of related diseases, herein termed "prostate cancer sequences." As outlined below, prostate cancer sequences include those that are up-regulated (i.e., expressed at a higher level) in prostate cancer, as well as those that are down-regulated (i.e.,
10 expressed at a lower level). In a preferred embodiment, the prostate cancer sequences are from humans; however, as will be appreciated by those in the art, prostate cancer sequences from other organisms may be useful in animal models of disease and drug evaluation; thus, other prostate cancer sequences are provided, from vertebrates, including mammals, including rodents (rats, mice, hamsters, guinea pigs, etc.), primates, farm animals (including
15 sheep, goats, pigs, cows, horses, etc.) and pets, e.g., (dogs, cats, etc.). Prostate cancer sequences from other organisms may be obtained using the techniques outlined below.

Prostate cancer sequences can include both nucleic acid and amino acid sequences. As will be appreciated by those in the art and is more fully outlined below, prostate cancer nucleic acid sequences are useful in a variety of applications, including diagnostic
20 applications, which will detect naturally occurring nucleic acids, as well as screening applications; e.g., biochips comprising nucleic acid probes or PCR microtiter plates with selected probes to the prostate cancer sequences can be generated.

A prostate cancer sequence can be initially identified by substantial nucleic acid and/or amino acid sequence homology to the prostate cancer sequences outlined herein. Such
25 homology can be based upon the overall nucleic acid or amino acid sequence, and is generally determined as outlined below, using either homology programs or hybridization conditions.

For identifying prostate cancer-associated sequences, the prostate cancer screen typically includes comparing genes identified in different tissues, e.g., normal and cancerous
30 tissues, or tumor tissue samples from patients who have metastatic disease vs. non metastatic tissue. Other suitable tissue comparisons include comparing prostate cancer samples with metastatic cancer samples from other cancers, such as lung, breast, gastrointestinal cancers,

ovarian, etc. Samples of different stages of prostate cancer, e.g., survivor tissue, drug resistant states, and tissue undergoing metastasis, are applied to biochips comprising nucleic acid probes. The samples are first microdissected, if applicable, and treated as is known in the art for the preparation of mRNA. Suitable biochips are commercially available, e.g., from

5 Affymetrix. Gene expression profiles are generated and the data analyzed.

In one embodiment, the genes showing changes in expression as between normal and disease states are compared to genes expressed in other normal tissues, preferably normal prostate, but also including, and not limited to lung, heart, brain, liver, breast, kidney, muscle, colon, small intestine, large intestine, spleen, bone, and placenta. In a preferred embodiment,

10 those genes identified during the prostate cancer screen that are expressed in a significant amount in other tissues are removed from the profile, although in some embodiments, this is not necessary. That is, when screening for drugs, it is usually preferable that the target be disease specific, to minimize possible side effects on other organs were there expression.

In a preferred embodiment, prostate cancer sequences are those that are up-regulated in prostate cancer or related conditions; that is, the expression of these genes is higher in the prostate cancer tissue as compared to non-cancerous tissue. "Up-regulation" as used herein often means at least about a two-fold change, preferably at least about a three fold change, with at least about five-fold or higher being preferred. Another embodiment is directed to sequences up-regulated in non-malignant conditions relative to normal.

20 Unigene cluster identification numbers and accession numbers herein are for the GenBank sequence database and the sequences of the accession numbers are hereby expressly incorporated by reference. GenBank is known in the art, see, e.g., Benson, et al. (1998) *Nucleic Acids Research* 26:1-7 and <http://www.ncbi.nlm.nih.gov/>. Sequences are also available in other databases, e.g., European Molecular Biology Laboratory (EMBL) and

25 DNA Database of Japan (DDBJ). U.S. Patent Application N. 09/687,576 and 09/976,858 (-001-3) further disclose related sequences, compositions, and methods of diagnosis and treatment of prostate cancer and related conditions and are hereby expressly incorporated by reference.

In another preferred embodiment, prostate cancer sequences are those that are down-regulated in the prostate cancer; that is, the expression of these genes is lower in prostate

30 cancer tissue as compared to non-cancerous tissue. "Down-regulation" as used herein often

means at least about a two-fold change, preferably at least about a three fold change, with at least about five-fold or higher being preferred.

Informatics

5 The ability to identify genes that are over or under expressed in prostate cancer can additionally provide high-resolution, high-sensitivity datasets which can be used in the areas of diagnostics, therapeutics, drug development, pharmacogenetics, protein structure, biosensor development, and other related areas. For example, the expression profiles can be used in diagnostic or prognostic evaluation of patients with prostate cancer. Or as another
10 example, subcellular toxicological information can be generated to better direct drug structure and activity correlation (see Anderson, Pharmaceutical Proteomics: Targets, Mechanism, and Function, paper presented at the IBC Proteomics conference, Coronado, CA (June 11-12, 1998)). Subcellular toxicological information can also be utilized in a biological sensor device to predict the likely toxicological effect of chemical exposures and likely tolerable
15 exposure thresholds (see U.S. Patent No. 5,811,231). Similar advantages accrue from datasets relevant to other biomolecules and bioactive agents (e.g., nucleic acids, saccharides, lipids, drugs, and the like).

Thus, in another embodiment, the present invention provides a database that includes at least one set of assay data. The data contained in the database is acquired, e.g., using array
20 analysis either singly or in a library format. The database can be in a form in which data can be maintained and transmitted, but is preferably an electronic database. The electronic database of the invention can be maintained on an electronic device allowing for the storage of and access to the database, such as a personal computer, but is preferably distributed on a wide area network, such as the World Wide Web.

25 The focus of the present section on databases that include peptide sequence data is for clarity of illustration only. It will be apparent to those of skill in the art that similar databases can be assembled for assay data acquired using an assay of the invention.

The compositions and methods for identifying and/or quantitating the relative and/or absolute abundance of a variety of molecular and macromolecular species from a biological
30 sample undergoing prostate cancer, i.e., the identification of prostate cancer-associated sequences described herein, provide an abundance of information, which can be correlated with pathological conditions, predisposition to disease, drug testing, therapeutic monitoring,

gene-disease causal linkages, identification of correlates of immunity and physiological status, among others. Although the data generated from the assays of the invention is suited for manual review and analysis, in a preferred embodiment, prior data processing using high-speed computers is utilized.

5 An array of methods for indexing and retrieving biomolecular information is known in the art. For example, U.S. Patents 6,023,659 and 5,966,712 disclose a relational database system for storing biomolecular sequence information in a manner that allows sequences to be catalogued and searched according to one or more protein function hierarchies. U.S. Patent 5,953,727 discloses a relational database having sequence records containing
10 information in a format that allows a collection of partial-length DNA sequences to be catalogued and searched according to association with one or more sequencing projects for obtaining full-length sequences from the collection of partial length sequences. U.S. Patent 5,706,498 discloses a gene database retrieval system for making a retrieval of a gene sequence similar to a sequence data item in a gene database based on the degree of similarity
15 between a key sequence and a target sequence. U.S. Patent 5,538,897 discloses a method using mass spectroscopy fragmentation patterns of peptides to identify amino acid sequences in computer databases by comparison of predicted mass spectra with experimentally-derived mass spectra using a closeness-of-fit measure. U.S. Patent 5,926,818 discloses a multi-dimensional database comprising a functionality for multi-dimensional data analysis
20 described as on-line analytical processing (OLAP), which entails the consolidation of projected and actual data according to more than one consolidation path or dimension. U.S. Patent 5,295,261 reports a hybrid database structure in which the fields of each database record are divided into two classes, navigational and informational data, with navigational fields stored in a hierarchical topological map which can be viewed as a tree structure or as
25 the merger of two or more such tree structures.

See also Mount, et al. (2001) Bioinformatics CSH Press; Durbin, et al. (eds. 1999) Biological Sequence Analysis: Probabilistic Models of Proteins and Nucleic Acids Cambridge Univ. Press; Baxeavanis and Ouellette (eds., 1998) Bioinformatics: A Practical Guide to the Analysis of Genes and Proteins Wiley-Liss; Rashidi and Buehler (1999)
30 Bioinformatics: Basic Applications in Biological Science and Medicine CRC Press; Setubal, et al. (eds. 1997) Introduction to Computational Molecular Biology Brooks/Cole; Misener and Krawetz (eds. 2000) Bioinformatics: Methods and Protocols Human Press; Higgins and

Taylor (eds. 2000) Bioinformatics: Sequence, Structure, and Databanks: A Practical Approach Oxford Univ. Press; Brown (2001) Bioinformatics: A Biologist's Guide to Biocomputing and the Internet Eaton Pub; Han and Kamber (2000) Data Mining: Concepts and Techniques Kaufmann Pub.; and Waterman (1995) Introduction to Computational Biology: Maps, Sequences, and Genomes Chap and Hall.

The present invention provides a computer database comprising a computer and software for storing in computer-retrievable form assay data records cross-tabulated, e.g., with data specifying the source of the target-containing sample from which each sequence specificity record was obtained.

In an exemplary embodiment, at least one of the sources of target-containing sample is from a control tissue sample known to be free of pathological disorders. In a variation, at least one of the sources is a known pathological tissue specimen, e.g., a neoplastic lesion or another tissue specimen to be analyzed for prostate cancer. In another variation, the assay records cross-tabulate one or more of the following parameters for each target species in a sample: (1) a unique identification code, which can include, e.g., a target molecular structure and/or characteristic separation coordinate (e.g., electrophoretic coordinates); (2) sample source; and (3) absolute and/or relative quantity of the target species present in the sample.

The invention also provides for the storage and retrieval of a collection of target data in a computer data storage apparatus, which can include magnetic disks, optical disks, magneto-optical disks, DRAM, SRAM, SGRAM, SDRAM, RDRAM, DDR RAM, magnetic bubble memory devices, and other data storage devices, including CPU registers and on-CPU data storage arrays. Typically, the target data records are stored as a bit pattern in an array of magnetic domains on a magnetizable medium or as an array of charge states or transistor gate states, such as an array of cells in a DRAM device (e.g., each cell comprised of a transistor and a charge storage area, which may be on the transistor). In one embodiment, the invention provides such storage devices, and computer systems built therewith, comprising a bit pattern encoding a protein expression fingerprint record comprising unique identifiers for at least 10 target data records cross-tabulated with target source.

When the target is a peptide or nucleic acid, the invention preferably provides a method for identifying related peptide or nucleic acid sequences, comprising performing a computerized comparison between a peptide or nucleic acid sequence assay record stored in or retrieved from a computer storage device or database and at least one other sequence. The

comparison can include a sequence analysis or comparison algorithm or computer program embodiment thereof (e.g., FASTA, TFASTA, GAP, BESTFIT) and/or the comparison may be of the relative amount of a peptide or nucleic acid sequence in a pool of sequences determined from a polypeptide or nucleic acid sample of a specimen.

5 The invention also preferably provides a magnetic disk, such as an IBM-compatible (DOS, Windows, Windows95/98/2000, Windows NT, OS/2) or other format (e.g., Linux, SunOS, Solaris, AIX, SCO Unix, VMS, MV, Macintosh, etc.) floppy diskette or hard (fixed, Winchester) disk drive, comprising a bit pattern encoding data from an assay of the invention in a file format suitable for retrieval and processing in a computerized sequence analysis,
10 comparison, or relative quantitation method.

The invention also provides a network, comprising a plurality of computing devices linked via a data link, such as an Ethernet cable (coax or 10BaseT), telephone line, ISDN line, wireless network, optical fiber, or other suitable signal transmission medium, whereby at least one network device (e.g., computer, disk array, etc.) comprises a pattern of magnetic
15 domains (e.g., magnetic disk) and/or charge domains (e.g., an array of DRAM cells) composing a bit pattern encoding data acquired from an assay of the invention.

The invention also provides a method for transmitting assay data that includes generating an electronic signal on an electronic communications device, such as a modem, ISDN terminal adapter, DSL, cable modem, ATM switch, or the like, wherein the signal
20 includes (in native or encrypted format) a bit pattern encoding data from an assay or a database comprising a plurality of assay results obtained by the method of the invention.

In a preferred embodiment, the invention provides a computer system for comparing a query target to a database containing an array of data structures, such as an assay result obtained by the method of the invention, and ranking database targets based on the degree of
25 identity and gap weight to the target data. A central processor is preferably initialized to load and execute the computer program for alignment and/or comparison of the assay results. Data for a query target is entered into the central processor via an I/O device. Execution of the computer program results in the central processor retrieving the assay data from the data file, which comprises a binary description of an assay result.

30 The target data or record and the computer program can be transferred to secondary memory, which is typically random access memory (e.g., DRAM, SRAM, SGRAM, or SDRAM). Targets are ranked according to the degree of correspondence between a selected

assay characteristic (e.g., binding to a selected affinity moiety) and the same characteristic of the query target and results are output via an I/O device. For example, a central processor can be a conventional computer (e.g., Intel Pentium, PowerPC, Alpha, PA-8000, SPARC, MIPS 4400, MIPS 10000, VAX, etc.); a program can be a commercial or public domain molecular biology software package (e.g., UWGCG Sequence Analysis Software, Darwin); a data file can be an optical or magnetic disk, a data server, a memory device (e.g., DRAM, SRAM, SGRAM, SDRAM, EPROM, bubble memory, flash memory, etc.); an I/O device can be a terminal comprising a video display and a keyboard, a modem, an ISDN terminal adapter, an Ethernet port, a punched card reader, a magnetic strip reader, or other suitable I/O device.

The invention also preferably provides the use of a computer system, such as that described above, which comprises: (1) a computer; (2) a stored bit pattern encoding a collection of peptide sequence specificity records obtained by the methods of the invention, which may be stored in the computer; (3) a comparison target, such as a query target; and (4) a program for alignment and comparison, typically with rank-ordering of comparison results on the basis of computed similarity values.

Characteristics of prostate cancer-associated proteins

Prostate cancer proteins of the present invention may be classified as secreted proteins, transmembrane proteins, or intracellular proteins. In one embodiment, the prostate cancer protein is an intracellular protein. Intracellular proteins may be found in the cytoplasm and/or in the nucleus. Intracellular proteins are involved in all aspects of cellular function and replication (including, e.g., signaling pathways); aberrant expression of such proteins often results in unregulated or dysregulated cellular processes (see, e.g., Alberts (ed. 1994) Molecular Biology of the Cell (3d ed.) Garland. For example, many intracellular proteins have enzymatic activity such as protein kinase activity, protein phosphatase activity, protease activity, nucleotide cyclase activity, polymerase activity and the like. Intracellular proteins also serve as docking proteins that are involved in organizing complexes of proteins, or targeting proteins to various subcellular localizations, and are involved in maintaining the structural integrity of organelles.

An increasingly appreciated concept in characterizing proteins is the presence in the proteins of one or more structural motifs for which defined functions have been attributed. In

addition to the highly conserved sequences found in the enzymatic domain of proteins, highly conserved sequences have been identified in proteins that are involved in protein-protein interaction. For example, Src-homology-2 (SH2) domains bind tyrosine-phosphorylated targets in a sequence dependent manner. PTB domains, which are distinct from SH2 domains, also bind tyrosine phosphorylated targets. SH3 domains bind to proline-rich targets. In addition, PH domains, tetratricopeptide repeats and WD domains to name only a few, have been shown to mediate protein-protein interactions. Some of these may also be involved in binding to phospholipids or other second messengers. As will be appreciated by one of ordinary skill in the art, these motifs can be identified on the basis of amino acid sequence; thus, an analysis of the sequence of proteins may provide insight into both the enzymatic potential of the molecule and/or molecules with which the protein may associate. One useful database is Pfam (protein families), which is a large collection of multiple sequence alignments and hidden Markov models covering many common protein domains. Versions are available via the internet from Washington University in St. Louis, the Sanger Center in England, and the Karolinska Institute in Sweden (see, e.g., Bateman, et al. (2000) Nuc. Acids Res. 28:263-266; Sonnhammer, et al. (1997) Proteins 28:405-420; Bateman, et al. (1999) Nuc. Acids Res. 27:260-262; and Sonnhammer, et al. (1998) Nuc. Acids Res. 26:320-322.

In another embodiment, the prostate cancer sequences are transmembrane proteins. Transmembrane proteins are molecules that span a phospholipid bilayer of a cell. They may have an intracellular domain, an extracellular domain, or both. The intracellular domains of such proteins may have a number of functions including those already described for intracellular proteins. For example, the intracellular domain may have enzymatic activity and/or may serve as a binding site for additional proteins. Frequently the intracellular domain of transmembrane proteins serves both roles. For example certain receptor tyrosine kinases have both protein kinase activity and SH2 domains. In addition, autophosphorylation of tyrosines on the receptor molecule itself, creates binding sites for additional SH2 domain containing proteins.

Transmembrane proteins may contain from one to many transmembrane domains. For example, receptor tyrosine kinases, certain cytokine receptors, receptor guanylyl cyclases and receptor serine/threonine protein kinases contain a single transmembrane domain. However, various other proteins including channels and adenylyl cyclases contain numerous

transmembrane domains. Many important cell surface receptors such as G protein coupled receptors (GPCRs) are classified as "seven transmembrane domain" proteins, as they contain 7 membrane spanning regions. Characteristics of transmembrane domains include approximately 17 consecutive hydrophobic amino acids that may be followed by charged amino acids. Therefore, upon analysis of the amino acid sequence of a particular protein, the localization and number of transmembrane domains within the protein may be predicted (see, e.g., PSORT web site <http://psort.nibb.ac.jp/>). Important transmembrane protein receptors include, but are not limited to the insulin receptor, insulin-like growth factor receptor, human growth hormone receptor, glucose transporters, transferrin receptor, epidermal growth factor receptor, low density lipoprotein receptor, epidermal growth factor receptor, leptin receptor, and interleukin receptors, e.g., IL-1 receptor, IL-2 receptor, etc.

The extracellular domains of transmembrane proteins are diverse; however, conserved motifs are found repeatedly among various extracellular domains. Conserved structure and/or functions have been ascribed to different extracellular motifs. Many extracellular domains are involved in binding to other molecules. In one aspect, extracellular domains are found on receptors. Factors that bind the receptor domain include circulating ligands, which may be peptides, proteins, or small molecules such as adenosine and the like. For example, growth factors such as EGF, FGF, and PDGF are circulating growth factors that bind to their cognate receptors to initiate a variety of cellular responses. Other factors include cytokines, mitogenic factors, neurotrophic factors and the like. Extracellular domains also bind to cell-associated molecules. In this respect, they mediate cell-cell interactions. Cell-associated ligands can be tethered to the cell, e.g., via a glycosylphosphatidylinositol (GPI) anchor, or may themselves be transmembrane proteins. Extracellular domains also associate with the extracellular matrix and contribute to the maintenance of the cell structure.

Prostate cancer proteins that are transmembrane are particularly preferred in the present invention as they are readily accessible targets for immunotherapeutics, as are described herein. In addition, as outlined below, transmembrane proteins can be also useful in imaging modalities. Antibodies may be used to label such readily accessible proteins in situ. Alternatively, antibodies can also label intracellular proteins, in which case samples are typically permeabilized to provide access to intracellular proteins.. In addition, some membrane proteins can be processed to release a soluble protein, or to expose a residual

fragment. Released soluble proteins may be useful diagnostic markers, processed residual protein fragments may be useful prostate markers of disease.

It will also be appreciated by those in the art that a transmembrane protein can be made soluble by removing transmembrane sequences, e.g., through recombinant methods.

- 5 Furthermore, transmembrane proteins that have been made soluble can be made to be secreted through recombinant means by adding an appropriate signal sequence.

- In another embodiment, the prostate cancer proteins are secreted proteins; the secretion of which can be either constitutive or regulated. These proteins may have a signal peptide or signal sequence that targets the molecule to the secretory pathway. Secreted
- 10 proteins are involved in numerous physiological events; by virtue of their circulating nature, they often serve to transmit signals to various other cell types. The secreted protein may function in an autocrine manner (acting on the cell that secreted the factor), a paracrine manner (acting on cells in close proximity to the cell that secreted the factor), an endocrine manner (acting on cells at a distance, e.g., secretion into the blood stream), or an exocrine
- 15 manner (secretion, e.g., through a duct or to adjacent epithelial surface as sweat glands, sebaceous glands, pancreatic ducts, lacrimal glands, mammary glands, sweat producing glands of the ear, etc.). Thus secreted molecules find use in modulating or altering numerous aspects of physiology. Prostate cancer proteins that are secreted proteins are particularly preferred in the present invention as they serve as good targets for diagnostic markers, e.g., for blood,
- 20 plasma, serum, or stool tests. Those which are enzymes may be antibody or small molecule targets. Others may be useful as vaccine targets, e.g., via CTL mechanisms.

Use of prostate cancer nucleic acids

- As described above, prostate cancer sequence is initially identified by substantial
- 25 nucleic acid and/or amino acid sequence homology or linkage to the prostate cancer sequences outlined herein. Such homology can be based upon the overall nucleic acid or amino acid sequence, and is generally determined as outlined below, using either homology programs or hybridization conditions. Typically, linked sequences on a mRNA are found on the same molecule.

- 30 The prostate cancer nucleic acid sequences of the invention, e.g., the sequences in Tables 1A-4, can be fragments of larger genes, i.e., they are nucleic acid segments. "Genes" in this context includes coding regions, non-coding regions, and mixtures of coding and non-

coding regions. Accordingly, as will be appreciated by those in the art, using the sequences provided herein, extended sequences, in either direction, of the prostate cancer genes can be obtained, using techniques well known in the art for cloning either longer sequences or the full length sequences; see Ausubel, et al., *supra*. Much can be done by informatics and many sequences can be clustered to include multiple sequences corresponding to a single gene, e.g., systems such as UniGene (see, <http://www.ncbi.nlm.nih.gov/UniGene/>).

Once the prostate cancer nucleic acid is identified, it can be cloned and, if necessary, its constituent parts recombined to form the entire prostate cancer nucleic acid coding regions or the entire mRNA sequence. Once isolated from its natural source, e.g., contained within a plasmid or other vector or excised therefrom as a linear nucleic acid segment, the recombinant prostate cancer nucleic acid can be further-used as a probe to identify and isolate other prostate cancer nucleic acids, e.g., extended coding regions. It can also be used as a "precursor" nucleic acid to make modified or variant prostate cancer nucleic acids and proteins.

The prostate cancer nucleic acids of the present invention are used in several ways. In a first embodiment, nucleic acid probes to the prostate cancer nucleic acids are made and attached to biochips to be used in screening and diagnostic methods, as outlined below, or for administration, e.g., for gene therapy, vaccine, and/or antisense applications. Alternatively, the prostate cancer nucleic acids that include coding regions of prostate cancer proteins can be put into expression vectors for the expression of prostate cancer proteins, again for screening purposes or for administration to a patient.

In a preferred embodiment, nucleic acid probes to prostate cancer nucleic acids (both the nucleic acid sequences outlined in the figures and/or the complements thereof) are made. The nucleic acid probes attached to the biochip are designed to be substantially complementary to the prostate cancer nucleic acids, i.e., the target sequence (either the target sequence of the sample or to other probe sequences, e.g., in sandwich assays), such that hybridization of the target sequence and the probes of the present invention occurs. As outlined below, this complementarity need not be perfect; there may be base pair mismatches which will interfere with hybridization between the target sequence and the single stranded nucleic acids of the present invention. However, if the number of mutations is so great that no hybridization can occur under even the least stringent of hybridization conditions, the sequence is not a complementary target sequence. Thus, by "substantially complementary"

herein is meant that the probes are sufficiently complementary to the target sequences to hybridize under normal reaction conditions, particularly high stringency conditions, as outlined herein.

A nucleic acid probe is generally single stranded but can be partially single and
5 partially double stranded. The strandedness of the probe is dictated by the structure, composition, and properties of the target sequence. In general, the nucleic acid probes range from about 8 to about 100 bases long, with from about 10 to about 80 bases being preferred, and from about 30 to about 50 bases being particularly preferred. That is, generally whole genes are not used. In some embodiments, much longer nucleic acids can be used, up to
10 hundreds of bases.

In a preferred embodiment, more than one probe per sequence is used, with either overlapping probes or probes to different sections of the target being used. That is, two, three, four or more probes, with three being preferred, are used to build in a redundancy for a particular target. The probes can be overlapping (i.e., have some sequence in common), or
15 separate. In some cases, PCR primers may be used to amplify signal for higher sensitivity.

As will be appreciated by those in the art, nucleic acids can be attached or immobilized to a solid support in a wide variety of ways. By "immobilized" and grammatical equivalents herein is meant the association or binding between the nucleic acid probe and the solid support is sufficient to be stable under the conditions of binding, washing, analysis, and
20 removal as outlined below. The binding can typically be covalent or non-covalent. By "non-covalent binding" and grammatical equivalents herein is meant one or more of electrostatic, hydrophilic, and hydrophobic interactions. Included in non-covalent binding is the covalent attachment of a molecule, such as, streptavidin to the support and the non-covalent binding of the biotinylated probe to the streptavidin. By "covalent binding" and grammatical
25 equivalents herein is meant that the two moieties, the solid support and the probe, are attached by at least one bond, including sigma bonds, pi bonds and coordination bonds. Covalent bonds can be formed directly between the probe and the solid support or can be formed by a cross linker or by inclusion of a specific reactive group on either the solid support or the probe or both molecules. Immobilization may also involve a combination of
30 covalent and non-covalent interactions.

In general, the probes are attached to the biochip in a wide variety of ways, as will be appreciated by those in the art. As described herein, the nucleic acids can either be

synthesized first, with subsequent attachment to the biochip, or can be directly synthesized on the biochip.

The biochip comprises a suitable solid substrate. By "substrate" or "solid support" or other grammatical equivalents herein is meant a material that can be modified to contain discrete individual sites appropriate for the attachment or association of the nucleic acid probes and is amenable to at least one detection method. As will be appreciated by those in the art, the number of possible substrates are very large, and include, but are not limited to, glass and modified or functionalized glass, plastics (including acrylics, polystyrene and copolymers of styrene and other materials, polypropylene, polyethylene, polybutylene, polyurethanes, Teflon, etc.), polysaccharides, nylon or nitrocellulose, resins, silica or silica-based materials including silicon and modified silicon, carbon, metals, inorganic glasses, plastics, etc. In general, the substrates allow optical detection and do not appreciably fluoresce. A preferred substrate is described in WO0055627, herein incorporated by reference in its entirety.

Generally the substrate is planar, although as will be appreciated by those in the art, other configurations of substrates may be used as well. For example, the probes may be placed on the inside surface of a tube, for flow-through sample analysis to minimize sample volume. Similarly, the substrate may be flexible, such as a flexible foam, including closed cell foams made of particular plastics.

In a preferred embodiment, the surface of the biochip and the probe may be derivatized with chemical functional groups for subsequent attachment of the two. Thus, e.g., the biochip is derivatized with a chemical functional group including, but not limited to, amino groups, carboxy groups, oxo groups and thiol groups, with amino groups being particularly preferred. Using these functional groups, the probes can be attached using functional groups on the probes. For example, nucleic acids containing amino groups can be attached to surfaces comprising amino groups, e.g., using linkers as are known in the art; e.g., homo- or hetero-bifunctional linkers as are well known (see 1994 Pierce Chemical Company catalog, technical section on cross-linkers, pages 155-200). In addition, in some cases, additional linkers, such as alkyl groups (including substituted and heteroalkyl groups) may be used.

In this embodiment, oligonucleotides are synthesized as is known in the art, and then attached to the surface of the solid support. As will be appreciated by those skilled in the art,

either the 5' or 3' terminus may be attached to the solid support, or attachment may be via an internal nucleoside.

In another embodiment, the immobilization to the solid support may be very strong, yet non-covalent. For example, biotinylated oligonucleotides can be made, which bind to surfaces covalently coated with streptavidin, resulting in attachment.

Alternatively, the oligonucleotides may be synthesized on the surface, as is known in the art. For example, photoactivation techniques utilizing photopolymerization compounds and techniques are used. In a preferred embodiment, the nucleic acids can be synthesized in situ, using well known photolithographic techniques, such as those described in WO 95/25116; WO 95/35505; U.S. Patent Nos. 5,700,637 and 5,445,934; and references cited within, all of which are expressly incorporated by reference; these methods of attachment form the basis of the Affymetrix GeneChip™ technology.

Often, amplification-based assays are performed to measure the expression level of prostate cancer-associated sequences. These assays are typically performed in conjunction with reverse transcription. In such assays, a prostate cancer-associated nucleic acid sequence acts as a template in an amplification reaction (e.g., Polymerase Chain Reaction, or PCR). In a quantitative amplification, the amount of amplification product will be proportional to the amount of template in the original sample. Comparison to appropriate controls provides a measure of the amount of prostate cancer-associated RNA. Methods of quantitative amplification are well known to those of skill in the art. Detailed protocols for quantitative PCR are provided, e.g., in Innis, et al. (1990) PCR Protocols: A Guide to Methods and Applications Academic Press.

In some embodiments, a TaqMan based assay is used to measure expression. TaqMan based assays use a fluorogenic oligonucleotide probe that contains a 5' fluorescent dye and a 3' quenching agent. The probe hybridizes to a PCR product, but cannot itself be extended due to a blocking agent at the 3' end. When the PCR product is amplified in subsequent cycles, the 5' nuclease activity of the polymerase, e.g., AmpliTaq, results in the cleavage of the TaqMan probe. This cleavage separates the 5' fluorescent dye and the 3' quenching agent, thereby resulting in an increase in fluorescence as a function of amplification (see, e.g., literature provided by Perkin-Elmer, e.g., www2.perkin-elmer.com).

Other suitable amplification methods include, but are not limited to, ligase chain reaction (LCR) (see Wu and Wallace (1989) Genomics 4:560-569, Landegren, et al. (1988)

Science 241:1077-1080, and Barringer, et al. (1990) Gene 89:117-122), transcription amplification (Kwong, et al. (1989) Proc. Natl. Acad. Sci. USA 86:1173-1177), self-sustained sequence replication (Guatelli, et al. (1990) Proc. Nat. Acad. Sci. USA 87:1874-1878), dot PCR, and linker adapter PCR, etc.

5

Expression of prostate cancer proteins from nucleic acids

In a preferred embodiment, prostate cancer nucleic acids, e.g., encoding prostate cancer proteins are used to make a variety of expression vectors to express prostate cancer proteins which can then be used in screening assays, as described below. Expression vectors and recombinant DNA technology are well known to those of skill in the art (see, e.g., Ausubel, supra, and Fernandez and Hoeffler (eds. 1999) Gene Expression Systems Academic Press) and are used to express proteins. The expression vectors may be either self-replicating extrachromosomal vectors or vectors which integrate into a host genome. Generally, these expression vectors include transcriptional and translational regulatory nucleic acid operably linked to the nucleic acid encoding the prostate cancer protein. The term "control sequences" refers to DNA sequences used for the expression of an operably linked coding sequence in a particular host organism. Control sequences that are suitable for prokaryotes, e.g., include a promoter, optionally an operator sequence, and a ribosome binding site. Eukaryotic cells are known to utilize promoters, polyadenylation signals, and enhancers.

20 Nucleic acid is "operably linked" when it is placed into a functional relationship with another nucleic acid sequence. For example, DNA for a presequence or secretory leader is operably linked to DNA for a polypeptide if it is expressed as a preprotein that participates in the secretion of the polypeptide; a promoter or enhancer is operably linked to a coding sequence if it affects the transcription of the sequence; a ribosome binding site is operably linked to a coding sequence if it is positioned so as to facilitate translation, and sequences may be operably linked when they are physically linked on the same molecule. Generally, "operably linked" means that the DNA sequences being linked are contiguous, and, in the case of a secretory leader, contiguous and in reading phase. However, enhancers do not have to be contiguous. Linking is typically accomplished by ligation at convenient restriction sites. If such sites do not exist, synthetic oligonucleotide adaptors or linkers are used in accordance with conventional practice. Transcriptional and translational regulatory nucleic acid will generally be appropriate to the host cell used to express the prostate cancer protein.

30

Numerous types of appropriate expression vectors, and suitable regulatory sequences are known in the art for a variety of host cells.

In general, transcriptional and translational regulatory sequences may include, but are not limited to, promoter sequences, ribosomal binding sites, transcriptional start and stop sequences, translational start and stop sequences, and enhancer or activator sequences. In a preferred embodiment, the regulatory sequences include a promoter and transcriptional start and stop sequences.

Promoter sequences encode either constitutive or inducible promoters. The promoters may be either naturally occurring promoters or hybrid promoters. Hybrid promoters, which combine elements of more than one promoter, are also known in the art, and are useful in the present invention.

In addition, an expression vector may comprise additional elements. For example, the expression vector may have two replication systems, thus allowing it to be maintained in two organisms, e.g., in mammalian or insect cells for expression and in a prokaryotic host for cloning and amplification. Furthermore, for integrating expression vectors, the expression vector contains at least one sequence homologous to the host cell genome, and preferably two homologous sequences which flank the expression construct. The integrating vector may be directed to a specific locus in the host cell by selecting the appropriate homologous sequence for inclusion in the vector. Constructs for integrating vectors are well known in the art (e.g., Fernandez and Hoeffler, supra).

In addition, in a preferred embodiment, the expression vector contains a selectable marker gene to allow the selection of transformed host cells. Selection genes are well known in the art and will vary with the host cell used.

The prostate cancer proteins of the present invention are produced by culturing a host cell transformed with an expression vector containing nucleic acid encoding a prostate cancer protein, under the appropriate conditions to induce or cause expression of the prostate cancer protein. Conditions appropriate for prostate cancer protein expression will vary with the choice of the expression vector and the host cell, and will be easily ascertained by one skilled in the art through routine experimentation or optimization. For example, the use of constitutive promoters in the expression vector will require optimizing the growth and proliferation of the host cell, while the use of an inducible promoter requires the appropriate growth conditions for induction. In addition, in some embodiments, the timing of the harvest

is important. For example, the baculoviral systems used in insect cell expression are lytic viruses, and thus harvest time selection can be crucial for product yield.

Appropriate host cells include yeast, bacteria, archaeobacteria, fungi, and insect and animal cells, including mammalian cells. Of particular interest are *Saccharomyces cerevisiae* and other yeasts, *E. coli*, *Bacillus subtilis*, Sf9 cells, C129 cells, 293 cells, *Neurospora*, BHK, CHO, COS, HeLa cells, HUVEC (human umbilical vein endothelial cells), THP1 cells (a macrophage cell line) and various other human cells and cell lines.

In a preferred embodiment, the prostate cancer proteins are expressed in mammalian cells. Mammalian expression systems are also known in the art, and include retroviral and adenoviral systems. One expression vector system is a retroviral vector system such as is generally described in PCT/US97/01019 and PCT/US97/01048, both of which are hereby expressly incorporated by reference. Of particular use as mammalian promoters are the promoters from mammalian viral genes, since the viral genes are often highly expressed and have a broad host range. Examples include the SV40 early promoter, mouse mammary tumor virus LTR promoter, adenovirus major late promoter, herpes simplex virus promoter, and the CMV promoter (see, e.g., Fernandez and Hoeffler, *supra*). Typically, transcription termination and polyadenylation sequences recognized by mammalian cells are regulatory regions located 3' to the translation stop codon and thus, together with the promoter elements, flank the coding sequence. Examples of transcription terminator and polyadenylation signals include those derived from SV40.

The methods of introducing exogenous nucleic acid into mammalian hosts, as well as other hosts, is well known in the art, and will vary with the host cell used. Techniques include dextran-mediated transfection, calcium phosphate precipitation, polybrene mediated transfection, protoplast fusion, electroporation, viral infection, encapsulation of the polynucleotide(s) in liposomes, and direct microinjection of the DNA into nuclei.

In a preferred embodiment, prostate cancer proteins are expressed in bacterial systems. Bacterial expression systems are well known in the art. Promoters from bacteriophage may also be used and are known in the art. In addition, synthetic promoters and hybrid promoters are also useful; e.g., the tac promoter is a hybrid of the trp and lac promoter sequences. Furthermore, a bacterial promoter can include naturally occurring promoters of non-bacterial origin that have the ability to bind bacterial RNA polymerase and initiate transcription. In addition to a functioning promoter sequence, an efficient ribosome

binding site is desirable. The expression vector may also include a signal peptide sequence that provides for secretion of the prostate cancer protein in bacteria. The protein is either secreted into the growth media (gram-positive bacteria) or into the periplasmic space, located between the inner and outer membrane of the cell (gram-negative bacteria). The bacterial expression vector may also include a selectable marker gene to allow for the selection of bacterial strains that have been transformed. Suitable selection genes include genes which render the bacteria resistant to drugs such as ampicillin, chloramphenicol, erythromycin, kanamycin, neomycin and tetracycline. Selectable markers also include biosynthetic genes, such as those in the histidine, tryptophan and leucine biosynthetic pathways. These components are assembled into expression vectors. Expression vectors for bacteria are well known in the art, and include vectors for *Bacillus subtilis*, *E. coli*, *Streptococcus cremoris*, and *Streptococcus lividans*, among others (e.g., Fernandez and Hoefler, supra). The bacterial expression vectors are transformed into bacterial host cells using techniques well known in the art, such as calcium chloride treatment, electroporation, and others.

In one embodiment, prostate cancer proteins are produced in insect cells. Expression vectors for the transformation of insect cells, and in particular, baculovirus-based expression vectors, are well known in the art.

In a preferred embodiment, prostate cancer protein is produced in yeast cells. Yeast expression systems are well known in the art, and include expression vectors for *Saccharomyces cerevisiae*, *Candida albicans* and *C. maltosa*, *Hansenula polymorpha*, *Kluyveromyces fragilis* and *K. lactis*, *Pichia guilliermondii* and *P. pastoris*, *Schizosaccharomyces pombe*, and *Yarrowia lipolytica*.

The prostate cancer protein may also be made as a fusion protein, using techniques well known in the art. Thus, e.g., for the creation of monoclonal antibodies, if the desired epitope is small, the prostate cancer protein may be fused to a carrier protein to form an immunogen. Alternatively, the prostate cancer protein may be made as a fusion protein to increase expression, or for other reasons. For example, when the prostate cancer protein is a prostate cancer peptide, the nucleic acid encoding the peptide may be linked to other nucleic acid for expression purposes.

In a preferred embodiment, the prostate cancer protein is purified or isolated after expression. Prostate cancer proteins may be isolated or purified in a variety of ways known to those skilled in the art depending on what other components are present in the sample.

Standard purification methods include electrophoretic, molecular, immunological and chromatographic techniques, including ion exchange, hydrophobic, affinity, and reverse-phase HPLC chromatography, and chromatofocusing. For example, the prostate cancer protein may be purified using a standard anti-prostate cancer protein antibody column.

- 5 Ultrafiltration and diafiltration techniques, in conjunction with protein concentration, are also useful. For general guidance in suitable purification techniques, see Scopes (1982) Protein Purification Springer-Verlag. The degree of purification necessary will vary depending on the use of the prostate cancer protein. In some instances no purification will be necessary.

- 10 Once expressed and purified if necessary, the prostate cancer proteins and nucleic acids are useful in a number of applications. They may be used as immunoselection reagents, as vaccine reagents, as screening agents, etc.

Variants of prostate cancer proteins

- 15 In one embodiment, the prostate cancer proteins are derivative or variant prostate cancer proteins as compared to the wild-type sequence. That is, as outlined more fully below, the derivative prostate cancer peptide will often contain at least one amino acid substitution, deletion or insertion, with amino acid substitutions being particularly preferred. The amino acid substitution, insertion, or deletion may occur at most any residue within the prostate cancer peptide.

- 20 Also included within one embodiment of prostate cancer proteins of the present invention are amino acid sequence variants. These variants typically fall into one or more of three classes: substitutional, insertional, or deletional variants. These variants ordinarily are prepared by site specific mutagenesis of nucleotides in the DNA encoding the prostate cancer protein, using cassette or PCR mutagenesis or other techniques well known in the art, to
25 produce DNA encoding the variant, and thereafter expressing the DNA in recombinant cell culture as outlined above. However, variant prostate cancer protein fragments having up to about 100-150 residues may be prepared by in vitro synthesis using established techniques. Amino acid sequence variants are characterized by the predetermined nature of the variation, a feature that sets them apart from naturally occurring allelic or interspecies variation of the
30 prostate cancer protein amino acid sequence. The variants typically exhibit the same qualitative biological activity as the naturally occurring analogue, although variants can also be selected which have modified characteristics as will be more fully outlined below.

While the site or region for introducing an amino acid sequence variation is predetermined, the mutation per se need not be predetermined. For example, in order to optimize the performance of a mutation at a given site, random mutagenesis may be conducted at the target codon or region and the expressed prostate cancer variants screened for the optimal combination of desired activity. Techniques for making substitution mutations at predetermined sites in DNA having a known sequence are well known, e.g., M13 primer mutagenesis and PCR mutagenesis. Screening of the mutants is done using assays of prostate cancer protein activities.

Amino acid substitutions are typically of single residues; insertions usually will be on the order of from about 1 to 20 amino acids, although considerably larger insertions may be tolerated. Deletions range from about 1 to about 20 residues, although in some cases deletions may be much larger.

Substitutions, deletions, insertions or a combination thereof may be used to arrive at a final derivative. Generally these changes are done on a few amino acids to minimize the alteration of the molecule. However, larger changes may be tolerated in certain circumstances. When small alterations in the characteristics of the prostate cancer protein are desired, substitutions are generally made in accordance with the amino acid substitution relationships provided in the definition section.

The variants typically exhibit the same qualitative biological activity and will elicit the same immune response as the naturally-occurring analog, although variants also are selected to modify the characteristics of the prostate cancer proteins as needed. Alternatively, the variant may be designed such that the biological activity of the prostate cancer protein is altered. For example, glycosylation sites may be altered or removed.

Substantial changes in function or immunological identity are made by selecting substitutions that are less conservative than those described above. For example, substitutions may be made which more significantly affect: the structure of the polypeptide backbone in the area of the alteration, for example the alpha-helical or beta-sheet structure; the charge or hydrophobicity of the molecule at the target site; or the bulk of the side chain. The substitutions which in general are expected to produce the greatest changes in the polypeptide's properties are those in which (a) a hydrophilic residue, e.g., serinyl or threoninyl is substituted for (or by) a hydrophobic residue, e.g., leucyl, isoleucyl, phenylalanyl, valyl or alanyl; (b) a cysteine or proline is substituted for (or by) another residue; (c) a residue having

an electropositive side chain, e.g., lysyl, arginyl, or histidyl, is substituted for (or by) an electronegative residue, e.g., glutamyl or aspartyl; or (d) a residue having a bulky side chain, e.g., phenylalanine, is substituted for (or by) one not having a side chain, e.g., glycine.

Covalent modifications of prostate cancer polypeptides are included within the scope of this invention. One type of covalent modification includes reacting targeted amino acid residues of a prostate cancer polypeptide with an organic derivatizing agent that is capable of reacting with selected side chains or the N-or C-terminal residues of a prostate cancer polypeptide. Derivatization with bifunctional agents is useful, for instance, for crosslinking prostate cancer polypeptides to a water-insoluble support matrix or surface for use in the method for purifying anti-prostate cancer polypeptide antibodies or screening assays, as is more fully described below. Commonly used crosslinking agents include, e.g., 1,1-bis(diazoacetyl)-2-phenylethane, glutaraldehyde, N-hydroxysuccinimide esters, e.g., esters with 4-azidosalicylic acid, homobifunctional imidoesters, including disuccinimidyl esters such as 3,3'-dithiobis(succinimidylpropionate), bifunctional maleimides such as bis-N-maleimido-1,8-octane and agents such as methyl-3-((p-azidophenyl)dithio)propioimide.

Other modifications include deamidation of glutaminyl and asparaginyl residues to the corresponding glutamyl and aspartyl residues, respectively, hydroxylation of proline and lysine, phosphorylation of hydroxyl groups of serinyl, threonyl or tyrosyl residues, methylation of the amino groups of the lysine, arginine, and histidine side chains (e.g., pp. 79-86, Creighton (1983) Proteins: Structure and Molecular Properties Freeman), acetylation of the N-terminal amine, and amidation of a C-terminal carboxyl group.

Another type of covalent modification of the prostate cancer polypeptide included within the scope of this invention comprises altering the native glycosylation pattern of the polypeptide. "Altering the native glycosylation pattern" is intended for purposes herein to mean deleting one or more carbohydrate moieties found in native sequence prostate cancer polypeptide, and/or adding one or more glycosylation sites that are not present in the native sequence prostate cancer polypeptide. Glycosylation patterns can be altered in many ways. For example the use of different cell types to express prostate cancer-associated sequences can result in different glycosylation patterns.

Addition of glycosylation sites to prostate cancer polypeptides may also be accomplished by altering the amino acid sequence thereof. The alteration may be made, e.g., by the addition of, or substitution by, one or more serine or threonine residues to the native

sequence prostate cancer polypeptide (for O-linked glycosylation sites). The prostate cancer amino acid sequence may optionally be altered through changes at the DNA level, particularly by mutating the DNA encoding the prostate cancer polypeptide at preselected bases such that codons are generated that will translate into the desired amino acids.

5 Another means of increasing the number of carbohydrate moieties on the prostate cancer polypeptide is by chemical or enzymatic coupling of glycosides to the polypeptide. Such methods are described in the art, e.g., in WO 87/05330, and pp. 259-306 in Aplin and Wriston (1981) CRC Crit. Rev. Biochem.

Removal of carbohydrate moieties present on the prostate cancer polypeptide may be
10 accomplished chemically or enzymatically or by mutational substitution of codons encoding for amino acid residues that serve as targets for glycosylation. Chemical deglycosylation techniques are known in the art and described, e.g., by Hakimuddin, et al. (1987) Arch. Biochem. Biophys. 259:52-57; and Edge, et al. (1981) Anal. Biochem. 118:131-137. Enzymatic cleavage of carbohydrate moieties on polypeptides can be achieved by the use of a
15 variety of endo-and exo-glycosidases as described by Thotakura, et al. (1987) Meth. Enzymol. 138:350-359.

Another type of covalent modification of prostate cancer comprises linking the prostate cancer polypeptide to one of a variety of nonproteinaceous polymers, e.g., polyethylene glycol, polypropylene glycol, or polyoxyalkylenes, in the manner set forth in
20 U.S. Patent Nos. 4,640,835; 4,496,689; 4,301,144; 4,670,417; 4,791,192; or 4,179,337.

Prostate cancer polypeptides of the present invention may also be modified in a way to form chimeric molecules comprising a prostate cancer polypeptide fused to another, heterologous polypeptide or amino acid sequence. In one embodiment, such a chimeric molecule comprises a fusion of a prostate cancer polypeptide with a tag polypeptide which
25 provides an epitope to which an anti-tag antibody can selectively bind. The epitope tag is generally placed at the amino-or carboxyl-terminus of the prostate cancer polypeptide. The presence of such epitope-tagged forms of a prostate cancer polypeptide can be detected using an antibody against the tag polypeptide. Also, provision of the epitope tag enables the prostate cancer polypeptide to be readily purified by affinity purification using an anti-tag
30 antibody or another type of affinity matrix that binds to the epitope tag. In an alternative embodiment, the chimeric molecule may comprise a fusion of a prostate cancer polypeptide

with an immunoglobulin or a particular region of an immunoglobulin. For a bivalent form of the chimeric molecule, such a fusion could be to the Fc region of an IgG molecule.

Various tag polypeptides and their respective antibodies are well known in the art. Examples include poly-histidine (poly-his) or poly-histidine-glycine (poly-his-gly) tags; HIS6 and metal chelation tags, the flu HA tag polypeptide and its antibody 12CA5 (Field, et al. (1988) Mol. Cell. Biol. 8:2159-2165; the c-myc tag and the 8F9, 3C7, 6E10, G4, B7, and 9E10 antibodies thereto (Evan, et al. (1985) Molecular and Cellular Biology 5:3610-3616); and the Herpes Simplex virus glycoprotein D (gD) tag and its antibody (Paborsky, et al. (1990) Protein Engineering 3:547-553). Other tag polypeptides include the Flag-peptide (Hopp, et al. (1988) BioTechnology 6:1204-1210); the KT3 epitope peptide (Martin, et al. (1992) Science 255:192-194); tubulin epitope peptide (Skinner, et al. (1991) J. Biol. Chem. 266:15163-15166); and the T7 gene 10 protein peptide tag (Lutz-Freyermuth, et al. (1990) Proc. Natl. Acad. Sci. USA 87:6393-6397).

Also included are other prostate cancer proteins of the prostate cancer family, and prostate cancer proteins from other organisms, which are cloned and expressed as outlined below. Thus, probe or degenerate polymerase chain reaction (PCR) primer sequences may be used to find other related prostate cancer proteins from humans or other organisms. As will be appreciated by those in the art, particularly useful probe and/or PCR primer sequences include the unique areas of the prostate cancer nucleic acid sequence. As is generally known in the art, preferred PCR primers are from about 15 to about 35 nucleotides in length, with from about 20 to about 30 being preferred, and may contain inosine as needed. The conditions for the PCR reaction are well known in the art (e.g., Innis, PCR Protocols, supra).

Antibodies to prostate cancer proteins

In a preferred embodiment, when the prostate cancer protein is to be used to generate antibodies, e.g., for immunotherapy or immunodiagnosis, the prostate cancer protein should share at least one epitope or determinant with the full length protein. By "epitope" or "determinant" herein is typically meant a portion of a protein which will generate and/or bind an antibody or T-cell receptor in the context of MHC. Thus, in most instances, antibodies made to a smaller prostate cancer protein will be able to bind to the full-length protein, particularly linear epitopes. In a preferred embodiment, the epitope is unique; that is, antibodies generated to a unique epitope show little or no cross-reactivity.

Methods of preparing polyclonal antibodies are known to the skilled artisan (e.g., Coligan, *supra*; and Harlow and Lane, *supra*). Polyclonal antibodies can be raised in a mammal, e.g., by one or more injections of an immunizing agent and, if desired, an adjuvant. Typically, the immunizing agent and/or adjuvant will be injected in the mammal by multiple subcutaneous or intraperitoneal injections. The immunizing agent may include a protein encoded by a nucleic acid of the figures or fragment thereof or a fusion protein thereof. It may be useful to conjugate the immunizing agent to a protein known to be immunogenic in the mammal being immunized. Examples of such immunogenic proteins include but are not limited to keyhole limpet hemocyanin, serum albumin, bovine thyroglobulin, and soybean trypsin inhibitor. Examples of adjuvants which may be employed include Freund's complete adjuvant and MPL-TDM adjuvant (monophosphoryl Lipid A, synthetic trehalose dicorynomycolate). The immunization protocol may be selected by one skilled in the art without undue experimentation.

The antibodies may, alternatively, be monoclonal antibodies. Monoclonal antibodies may be prepared using hybridoma methods, such as those described by Kohler and Milstein (1975) *Nature* 256:495. In a hybridoma method, a mouse, hamster, or other appropriate host animal, is typically immunized with an immunizing agent to elicit lymphocytes that produce or are capable of producing antibodies that will specifically bind to the immunizing agent. Alternatively, the lymphocytes may be immunized in vitro. The immunizing agent will typically include a polypeptide encoded by a nucleic acid of Tables 1A-4 or fragment thereof, or a fusion protein thereof. Generally, either peripheral blood lymphocytes ("PBLs") are used if cells of human origin are desired, or spleen cells or lymph node cells are used if non-human mammalian sources are desired. The lymphocytes are then fused with an immortalized cell line using a suitable fusing agent, such as polyethylene glycol, to form a hybridoma cell (see pp. 59-103 in Goding (1986) Monoclonal Antibodies: Principles and Practice Academic Press). Immortalized cell lines are usually transformed mammalian cells, particularly myeloma cells of rodent, bovine and human origin. Usually, rat or mouse myeloma cell lines are employed. The hybridoma cells may be cultured in a suitable culture medium that preferably contains one or more substances that inhibit the growth or survival of the unfused, immortalized cells. For example, if the parental cells lack the enzyme hypoxanthine guanine phosphoribosyl transferase (HGPRT or HPRT), the culture medium

for the hybridomas typically will include hypoxanthine, aminopterin, and thymidine ("HAT medium"), which substances prevent the growth of HGPRT-deficient cells.

In one embodiment, the antibodies are bispecific antibodies. Bispecific antibodies are monoclonal, preferably human or humanized, antibodies that have binding specificities for at least two different antigens or that have binding specificities for two epitopes on the same antigen. In one embodiment, one of the binding specificities is for a protein encoded by a nucleic acid of Tables 1A-4 or a fragment thereof, the other one is for another antigen, and preferably for a cell-surface protein or receptor or receptor subunit, preferably one that is tumor specific. Alternatively, tetramer-type technology may create multivalent reagents.

In a preferred embodiment, the antibodies to prostate cancer protein are capable of reducing or eliminating a biological function of a prostate cancer protein, as is described below. That is, the addition of anti-prostate cancer protein antibodies (either polyclonal or preferably monoclonal) to prostate cancer tissue (or cells containing prostate cancer) may reduce or eliminate the prostate cancer. Generally, at least a 25% decrease in activity, growth, size or the like is preferred, with at least about 50% being particularly preferred and about a 95-100% decrease being especially preferred.

In a preferred embodiment the antibodies to the prostate cancer proteins are humanized antibodies (e.g., Xenerex Biosciences; Medarex, Inc.; Abgenix, Inc.; Protein Design Labs, Inc.). Humanized forms of non-human (e.g., murine) antibodies are chimeric molecules of immunoglobulins, immunoglobulin chains or fragments thereof (such as Fv, Fab, Fab', F(ab')₂ or other antigen-binding subsequences of antibodies) which contain minimal sequence derived from non-human immunoglobulin. Humanized antibodies include human immunoglobulins (recipient antibody) in which residues from a complementary determining region (CDR) of the recipient are replaced by residues from a CDR of a non-human species (donor antibody) such as mouse, rat or rabbit having the desired specificity, affinity and capacity. In some instances, Fv framework residues of the human immunoglobulin are replaced by corresponding non-human residues. Humanized antibodies may also comprise residues which are found neither in the recipient antibody nor in the imported CDR or framework sequences. In general, a humanized antibody will comprise substantially all of at least one, and typically two, variable domains, in which all or substantially all of the CDR regions correspond to those of a non-human immunoglobulin and all or substantially all of the framework (FR) regions are those of a human

immunoglobulin consensus sequence. The humanized antibody optimally also will comprise at least a portion of an immunoglobulin constant region (Fc), typically that of a human immunoglobulin (Jones, et al. (1986) Nature 321:522-525; Riechmann, et al. (1988) Nature 332:323-329; and Presta (1992) Curr. Op. Struct. Biol. 2:593-596). Humanization can be essentially performed following methods of Winter and co-workers (see, e.g., Jones, et al. (1986) Nature 321:522-525; Riechmann, et al. (1988) Nature 332:323-327; and Verhoeven, et al. (1988) Science 239:1534-1536), by substituting rodent CDRs or CDR sequences for the corresponding sequences of a human antibody. Accordingly, such humanized antibodies are chimeric antibodies (U.S. Patent No. 4,816,567), wherein substantially less than an intact human variable domain has been substituted by the corresponding sequence from a non-human species.

Human antibodies can also be produced using various techniques known in the art, including phage display libraries (Hoogenboom and Winter (1991) J. Mol. Biol. 227:381-388; Marks, et al. (1991) J. Mol. Biol. 222:581-597) or the preparation of human monoclonal antibodies (e.g., p77 in Cole, et al. (1985) Monoclonal Antibodies and Cancer Therapy Liss; and Boerner, et al. (1991) J. Immunol. 147(1):86-95). Similarly, human antibodies can be made by introducing of human immunoglobulin loci into transgenic animals, e.g., mice in which the endogenous immunoglobulin genes have been partially or completely inactivated. Upon challenge, human antibody production is observed, which closely resembles that seen in humans in most respects, including gene rearrangement, assembly, and antibody repertoire. This approach is described, e.g., in U.S. Patent Nos. 5,545,807; 5,545,806; 5,569,825; 5,625,126; 5,633,425; 5,661,016, and in the following scientific publications: Marks, et al. (1992) Bio/Technology 10:779-783; Lonberg, et al. (1994) Nature 368:856-859; Morrison (1994) Nature 368:812-13; Fishwild, et al. (1996) Nature Biotechnology 14:845-51; Neuberger (1996) Nature Biotechnology 14:826; Lonberg and Huszar (1995) Intern. Rev. Immunol. 13:65-93.

By immunotherapy is meant treatment of prostate cancer with an antibody raised against prostate cancer proteins. As used herein, immunotherapy can be passive or active. Passive immunotherapy as defined herein is the passive transfer of antibody to a recipient (patient). Active immunization is the induction of antibody and/or T-cell responses in a recipient (patient). Induction of an immune response is the result of providing the recipient with an antigen to which antibodies are raised. As appreciated by one of ordinary skill in the

art, the antigen may be provided by injecting a polypeptide against which antibodies are desired to be raised into a recipient, or contacting the recipient with a nucleic acid capable of expressing the antigen and under conditions for expression of the antigen, leading to an immune response.

5 In a preferred embodiment the prostate cancer proteins against which antibodies are raised are secreted proteins as described above. Without being bound by theory, antibodies used for treatment, bind and prevent the secreted protein from binding to its receptor, thereby inactivating the secreted prostate cancer protein.

10 In another preferred embodiment, the prostate cancer protein to which antibodies are raised is a transmembrane protein. Without being bound by theory, antibodies used for treatment bind the extracellular domain of the prostate cancer protein and prevent it from binding to other proteins, such as circulating ligands or cell-associated molecules. The antibody may cause down-regulation of the transmembrane prostate cancer protein. As will be appreciated by one of ordinary skill in the art, the antibody may be a competitive, non-competitive or uncompetitive inhibitor of protein binding to the extracellular domain of the prostate cancer protein. The antibody is also often an antagonist of the prostate cancer protein. Further, the antibody may prevent activation of the transmembrane prostate cancer protein. In one aspect, when the antibody prevents the binding of other molecules to the prostate cancer protein, the antibody prevents growth of the cell. The antibody may also be used to target or sensitize the cell to cytotoxic agents, including, but not limited to TNF- α , TNF- β , IL-1, TNF- γ , and IL-2, or chemotherapeutic agents including 5FU, vinblastine, actinomycin D, cisplatin, methotrexate, and the like. In some instances the antibody belongs to a sub-type that activates serum complement when complexed with the transmembrane protein thereby mediating cytotoxicity or antigen-dependent cytotoxicity (ADCC). Thus, 25 prostate cancer is treated by administering to a patient antibodies directed against the transmembrane prostate cancer protein. Antibody-labeling may activate a co-toxin, localize a toxin payload, or otherwise provide means to locally ablate cells.

In another preferred embodiment, the antibody is conjugated to an effector moiety. The effector moiety can be a labeling moiety such as a radioactive label or fluorescent label, 30 or can be a therapeutic moiety. In one aspect the therapeutic moiety is a small molecule that modulates the activity of the prostate cancer protein. In another aspect the therapeutic moiety modulates the activity of molecules associated with or in close proximity to the prostate

cancer protein. The therapeutic moiety may inhibit enzymatic activity such as protease or collagenase or protein kinase activity associated with prostate cancer.

In a preferred embodiment, the therapeutic moiety can also be a cytotoxic agent. In this method, targeting the cytotoxic agent to prostate cancer tissue or cells, results in a reduction in the number of afflicted cells, thereby reducing symptoms associated with prostate cancer. Cytotoxic agents are numerous and varied and include, but are not limited to, cytotoxic drugs or toxins or active fragments of such toxins. Suitable toxins and their corresponding fragments include diphtheria A chain, exotoxin A chain, ricin A chain, abrin A chain, curcin, crotin, phenomycin, enomycin, saporin, auristatin, and the like. Cytotoxic agents also include radiochemicals made by conjugating radioisotopes to antibodies raised against prostate cancer proteins, or binding of a radionuclide to a chelating agent that has been covalently attached to the antibody. Targeting the therapeutic moiety to transmembrane prostate cancer proteins not only serves to increase the local concentration of therapeutic moiety in the prostate cancer afflicted area, but also serves to reduce deleterious side effects, e.g., by binding to normal tissues, that may be associated with the therapeutic moiety.

In another preferred embodiment, the prostate cancer protein against which the antibodies are raised is an intracellular protein. In this case, the antibody may be conjugated to a protein which facilitates entry into the cell. In one case, the antibody enters the cell by endocytosis. In another embodiment, a nucleic acid encoding the antibody is administered to the individual or cell. Moreover, wherein the prostate cancer protein can be targeted within a cell, i.e., the nucleus, an antibody thereto contains a signal for that target localization, i.e., a nuclear localization signal.

The prostate cancer antibodies of the invention specifically bind to prostate cancer proteins. By "specifically bind" herein is meant that the antibodies bind to the protein with a K_d of at least about 0.1 mM, more usually at least about 1 μ M, preferably at least about 0.1 μ M or better, and most preferably, 0.01 μ M or better. Selectivity of binding is also important.

Detection of prostate cancer sequence for diagnostic and therapeutic applications

In one aspect, the RNA expression levels of genes are determined for different cellular states in the prostate cancer phenotype. After androgen ablation therapy, cells that survive the therapy undergo a period of quiescence followed at sometime later by active cell

division. As explained above, there are a variety of expression patterns characteristic of the prostate cancer genes involved in androgen-independent prostate cancer. Some genes are expressed early in the time course following ablation therapy, then drop off in expression, and then express again with emergence of androgen-independence (hi-lo-hi pattern in 1A).

Other genes are expressed early in the time course following ablation therapy, then drop off in expression, and do not express again with emergence of androgen-independence (hi-lo-lo pattern in Table 1A). Still other genes are not expressed early in the time course, but express only with emergence of androgen-independence (lo-lo-hi pattern in Table 1A). Other genes are not expressed early in the time course, but then express as androgen is withdrawn and continue to express with emergence of androgen-independence (lo-hi-hi pattern in Table 1A). Finally, some genes are not expressed early in the time course, but then express as androgen is withdrawn and drop off again with emergence of androgen-independence (lo-hi-lo pattern in Table 1A). Thus, the data suggest that different antigens are expressed in quiescent cells and actively dividing androgen-independent prostate cancer cells.

In another aspect, the RNA expression levels of genes are determined for different cellular states in the prostate cancer phenotype. After androgen ablation therapy, cells that survive the therapy undergo a period of quiescence followed at sometime later by active cell division. As explained above, there are a variety of expression patterns characteristic of the prostate cancer genes involved in androgen-independent prostate cancer. Some genes are expressed early in the time course following ablation therapy, then drop off in expression, and then express again with emergence of androgen-independence (hi-lo-lo-hi pattern in Table 2A). Other genes are expressed early in the time course following ablation therapy, then drop off in expression, and do not express again with emergence of androgen-independence (hi-lo-lo-lo and hi-hi-lo-lo pattern in Table 2A). Still other genes are not expressed early in the time course, but express only with emergence of androgen-independence (lo-lo-lo-hi pattern in Table 2A). Other genes are not expressed early in the time course, but then express as androgen is withdrawn and continue to express with emergence of androgen-independence (lo-lo-hi-hi pattern in Table 2A). Finally, some genes are not expressed early in the time course, but then express as androgen is withdrawn and drop off again with emergence of androgen-independence (lo-lo-hi-lo pattern in Table 2A). Thus, the data suggest that different antigens are expressed in quiescent cells (during androgen withdrawal) and actively dividing androgen-independent prostate cancer cells.

Effective therapy to combat androgen-independent prostate cancer requires that the timing of therapy coincide with expression of the target genes. Patients can be monitored for the expression of certain diagnostic antigens that indicate the presence of quiescent cells or which indicate the transition to actively dividing androgen-independent prostate cancer cells.

5 Thus, therapy to combat androgen-independent prostate cancer should begin at some time following androgen ablation therapy, depending on the particular target. Typically the transition from quiescence to actively dividing androgen-independent prostate cancer occurs between 6-24 months following androgen ablation therapy. Thus, preferred time periods for the therapies of the invention are as follows:

10 Expression levels of genes in normal tissue (i.e., not undergoing prostate cancer) and in prostate cancer tissue (and in some cases, for varying severities of prostate cancer that relate to prognosis, as outlined below) or in non-malignant disease are evaluated to provide expression profiles. An expression profile of a particular cell state or point of development is essentially a "fingerprint" of the state. While two states may have a particular gene similarly
15 expressed, the evaluation of a number of genes simultaneously allows the generation of a gene expression profile that is reflective of the state of the cell. By comparing expression profiles of cells in different states, information regarding which genes are important (including both up- and down-regulation of genes) in each of these states is obtained. Then, diagnosis may be performed or confirmed to determine whether a tissue sample has the gene
20 expression profile of normal or cancerous tissue. This will provide for molecular diagnosis of related conditions.

"Differential expression," or grammatical equivalents as used herein, refers to qualitative or quantitative differences in the temporal and/or cellular gene expression patterns within and among cells and tissue. Thus, a differentially expressed gene can qualitatively
25 have its expression altered, including an activation or inactivation, in, e.g., normal versus prostate cancer tissue. Genes may be turned on or turned off in a particular state, relative to another state thus permitting comparison of two or more states. A qualitatively regulated gene will exhibit an expression pattern within a state or cell type which is detectable by standard techniques. Some genes will be expressed in one state or cell type, but not in both.
30 Alternatively, the difference in expression may be quantitative, e.g., in that expression is increased or decreased; i.e., gene expression is either upregulated, resulting in an increased amount of transcript, or downregulated, resulting in a decreased amount of transcript. The

degree to which expression differs need only be large enough to quantify via standard characterization techniques as outlined below, such as by use of Affymetrix GeneChip™ expression arrays, Lockhart (1996) Nature Biotechnology 14:1675-1680, hereby expressly incorporated by reference. Other techniques include, but are not limited to, quantitative reverse transcriptase PCR, northern analysis and RNase protection. As outlined above, preferably the change in expression (i.e., upregulation or downregulation) is at least about 50%, more preferably at least about 100%, more preferably at least about 150%, more preferably at least about 200%, with from 300 to at least 1000% being especially preferred.

Evaluation may be at the gene transcript, or the protein level. The amount of gene expression may be monitored using nucleic acid probes to the DNA or RNA equivalent of the gene transcript, and the quantification of gene expression levels, or, alternatively, the final gene product itself (protein) can be monitored, e.g., with antibodies to the prostate cancer protein and standard immunoassays (ELISAs, etc.) or other techniques, including mass spectroscopy assays, 2D gel electrophoresis assays, etc. Proteins corresponding to prostate cancer genes, i.e., those identified as being important in a prostate cancer or disease phenotype, can be evaluated in a prostate cancer diagnostic test.

In a preferred embodiment, gene expression monitoring is performed simultaneously on a number of genes. Multiple protein expression monitoring can be performed as well. Similarly, these assays may be performed on an individual basis as well.

In this embodiment, the prostate cancer nucleic acid probes are attached to biochips as outlined herein for the detection and quantification of prostate cancer sequences in a particular cell. The assays are further described below in the example. PCR techniques can be used to provide greater sensitivity.

In a preferred embodiment nucleic acids encoding the prostate cancer protein are detected. Although DNA or RNA encoding the prostate cancer protein may be detected, of particular interest are methods wherein an mRNA encoding a prostate cancer protein is detected. Probes to detect mRNA can be a nucleotide/deoxynucleotide probe that is complementary to and hybridizes with the mRNA and includes, but is not limited to, oligonucleotides, cDNA, or RNA. Probes also should contain a detectable label, as defined herein. In one method the mRNA is detected after immobilizing the nucleic acid to be examined on a solid support such as nylon membranes and hybridizing the probe with the sample. Following washing to remove the non-specifically bound probe, the label is

detected. In another method detection of the mRNA is performed in situ (in situ hybridization or ISH). In this method permeabilized cells or tissue samples are contacted with a detectably labeled nucleic acid probe for sufficient time to allow the probe to hybridize with the target mRNA. Following washing to remove the non-specifically bound probe, the label is detected. For example a digoxigenin labeled riboprobe (RNA probe) that is complementary to the mRNA encoding a prostate cancer protein is detected by binding the digoxigenin with an anti-digoxigenin secondary antibody and developed with nitro blue tetrazolium and 5-bromo-4-chloro-3-indoyl phosphate.

In a preferred embodiment, various proteins from the three classes of proteins as described herein (secreted, transmembrane, or intracellular proteins) are used in diagnostic assays. The prostate cancer proteins, antibodies, nucleic acids, modified proteins and cells containing prostate cancer sequences are used in diagnostic assays. Such may evaluate tissues, e.g., immunohistochemistry, or evaluate body fluids, e.g., blood. The detection may be direct of cells, or indirect, e.g., of products from cells. This can be performed on an individual gene or corresponding polypeptide level. In a preferred embodiment, the expression profiles are used, preferably in conjunction with high throughput screening techniques to allow monitoring for expression profile genes and/or corresponding polypeptides.

As described and defined herein, prostate cancer proteins, including intracellular, transmembrane, or secreted proteins, find use as prognostic or diagnostic markers of prostate cancer or other prostate conditions. Detection of these proteins in putative prostate cancer tissue allows for detection, diagnosis, or prognosis of prostate proliferative disorders (malignant and non-malignant) including benign prostate hyperplasia (BPH) and cancer, and prostatitis. Diagnosis may also assist in selecting a therapeutic strategy, e.g., based on expression profiles and/or comparison to archival samples. In one embodiment, antibodies are used to detect prostate cancer proteins, directly or indirectly. A preferred method separates proteins from a sample by electrophoresis on a gel (typically a denaturing and reducing protein gel, but may be another type of gel, including isoelectric focusing gels and the like). Following separation of proteins, the prostate cancer protein is detected, e.g., by immunoblotting with antibodies raised against the prostate cancer protein. Methods of immunoblotting are well known to those of ordinary skill in the art.

In another preferred method, antibodies to the prostate cancer protein find use in in situ imaging techniques, e.g., in histology and/or in immunohistochemistry (e.g., Asai (ed. 1993) Methods in Cell Biology: Antibodies in Cell Biology (vol. 37) Academic Press. In this method cells are contacted with from one to many antibodies to the prostate cancer protein(s).

5 Following washing to remove non-specific antibody binding, the presence of the antibody or antibodies is detected. In one embodiment the antibody is detected by incubating with a secondary antibody that contains a detectable label. In another method the primary antibody to the prostate cancer protein(s) contains a detectable label, e.g., an enzyme marker that can act on a substrate. In another preferred embodiment each one of multiple primary antibodies

10 contains a distinct and detectable label. This method finds particular use in simultaneous screening for a plurality of prostate cancer proteins. As will be appreciated by one of ordinary skill in the art, many other histological imaging techniques are also provided by the invention.

In a preferred embodiment the label is detected in a fluorometer which has the ability

15 to detect and distinguish emissions of different wavelengths. In addition, a fluorescence activated cell sorter (FACS) can be used in the method.

In another preferred embodiment, antibodies find use in diagnosing prostate cancer from blood, serum, plasma, stool, and other samples. Such samples, therefore, are useful as samples to be probed or tested for the presence of prostate cancer proteins, which may be

20 diagnostic of prostate conditions beyond cancer, e.g., BPH. Antibodies can be used to detect a prostate cancer protein by previously described immunoassay techniques including ELISA, immunoblotting (western blotting), immunoprecipitation, BIACORE technology, and the like. Conversely, the presence of antibodies may indicate an immune response against an endogenous prostate cancer protein.

In a preferred embodiment, in situ hybridization of labeled prostate cancer nucleic acid probes to tissue arrays is done. For example, arrays of tissue samples, including prostate cancer tissue and/or normal tissue, are made. In situ hybridization (see, e.g., Ausubel, supra) is then performed. When comparing the fingerprints between an individual and a standard, the skilled artisan can make a diagnosis, a prognosis, or a prediction based on the findings. It

30 is further understood that the genes which indicate the diagnosis may differ from those which indicate the prognosis and molecular profiling of the condition of the cells may lead to distinctions between responsive or refractory conditions or may be predictive of outcomes.

In a preferred embodiment, the prostate cancer proteins, antibodies, nucleic acids, modified proteins, and cells containing prostate cancer sequences are used in prognosis assays. As above, gene expression profiles can be generated that correlate to prostate cancer or other prostate disorders, in terms of useful aspects of clinical condition, pathology, or other information which may be relevant to long term prognosis. Again, this may be done on either a protein or gene level, with the use of genes being preferred. Single or multiple genes may be useful in various combinations. As above, prostate cancer probes may be attached to biochips for the detection and quantification of prostate cancer sequences in a tissue or patient. The assays proceed as outlined above for diagnosis. PCR method may provide more sensitive and accurate quantification.

Assays for therapeutic compounds

In a preferred embodiment members of the proteins, nucleic acids, and antibodies as described herein are used in drug screening assays. The prostate cancer proteins, antibodies, nucleic acids, modified proteins, and cells containing prostate cancer sequences are used in drug screening assays or by evaluating the effect of drug candidates on a "gene expression profile" or expression profile of polypeptides. In a preferred embodiment, the expression profiles are used, preferably in conjunction with high throughput screening techniques to allow monitoring for expression profile genes after treatment with a candidate agent (e.g., Zlokarnik, et al. (1998) Science 279:84-88; Heid (1996) Genome Res. 6:986-94).

In a preferred embodiment, the prostate cancer proteins, antibodies, nucleic acids, modified proteins, and cells containing the native or modified prostate cancer proteins are used in screening assays. That is, the present invention provides novel methods for screening for compositions which modulate the prostate cancer phenotype or an identified physiological function of a prostate cancer protein. As above, this can be done on an individual gene level or by evaluating the effect of drug candidates on a "gene expression profile". In a preferred embodiment, the expression profiles are used, preferably in conjunction with high throughput screening techniques to allow monitoring for expression profile genes after treatment with a candidate agent, see Zlokarnik, supra.

Having identified the differentially expressed genes herein, a variety of assays may be executed. In a preferred embodiment, assays may be run on an individual gene or protein level. That is, having identified a particular gene as up regulated in prostate cancer, test

compounds can be screened for the ability to modulate gene expression or for binding to the prostate cancer protein. "Modulation" thus includes both an increase and a decrease in gene expression. The preferred amount of modulation will depend on the original change of the gene expression in normal versus tissue undergoing prostate cancer, with changes of at least 10%, preferably 50%, more preferably 100-300%, and in some embodiments 300-1000% or greater. Thus, if a gene exhibits a 4-fold increase in prostate cancer tissue compared to normal tissue, a decrease of about four-fold is often desired; similarly, a 10-fold decrease in prostate cancer tissue compared to normal tissue often provides a target value of a 10-fold increase in expression to be induced by the test compound.

The amount of gene expression may be monitored using nucleic acid probes and the quantification of gene expression levels, or, alternatively, the gene product itself can be monitored, e.g., through the use of antibodies to the prostate cancer protein and standard immunoassays. Proteomics and separation techniques may also allow quantification of expression.

In a preferred embodiment, gene expression or protein monitoring of a number of entities, i.e., an expression profile, is monitored simultaneously. Such profiles will typically involve a plurality of those entities described herein.

In this embodiment, the prostate cancer nucleic acid probes are attached to biochips as outlined herein for the detection and quantification of prostate cancer sequences in a particular cell. Alternatively, PCR may be used. Thus, a series, e.g., of microtiter plate, may be used with dispensed primers in desired wells. A PCR reaction can then be performed and analyzed for each well.

Expression monitoring can be performed to identify compounds that modify the expression of one or more prostate cancer-associated sequences, e.g., a polynucleotide sequence set out in Tables 1A-4. Generally, in a preferred embodiment, a test modulator is added to the cells prior to analysis. Moreover, screens are also provided to identify agents that modulate prostate cancer, modulate prostate cancer proteins, bind to a prostate cancer protein, or interfere with the binding of a prostate cancer protein and an antibody or other binding partner.

The term "test compound" or "drug candidate" or "modulator" or grammatical equivalents as used herein describes a molecule, e.g., protein, oligopeptide, small organic molecule, polysaccharide, polynucleotide, etc., to be tested for the capacity to directly or

indirectly alter the prostate cancer phenotype or the expression of a prostate cancer sequence, e.g., a nucleic acid or protein sequence. In preferred embodiments, modulators alter expression profiles, or expression profile nucleic acids or proteins provided herein. In one embodiment, the modulator suppresses a prostate cancer phenotype, e.g., to a normal or non-malignant tissue fingerprint. In another embodiment, a modulator induced a prostate cancer phenotype. Generally, a plurality of assay mixtures are run in parallel with different agent concentrations to obtain a differential response to the various concentrations. Typically, one of these concentrations serves as a negative control, i.e., at zero concentration or below the level of detection.

Drug candidates encompass numerous chemical classes, though typically they are organic molecules, preferably small organic compounds having a molecular weight of more than 100 and less than about 2,500 daltons. Preferred small molecules are less than 2000, or less than 1500, or less than 1000, or less than 500 D. Candidate agents comprise functional groups necessary for structural interaction with proteins, particularly hydrogen bonding, and typically include at least an amine, carbonyl, hydroxyl or carboxyl group, preferably at least two of the functional chemical groups. The candidate agents often comprise cyclical carbon or heterocyclic structures and/or aromatic or polyaromatic structures substituted with one or more of the above functional groups. Candidate agents are also found among biomolecules including peptides, saccharides, fatty acids, steroids, purines, pyrimidines, derivatives, structural analogs, or combinations thereof. Particularly preferred are peptides.

In one aspect, a modulator will neutralize the effect of a prostate cancer protein. By "neutralize" is meant that activity of a protein is inhibited or blocked and the consequent effect on the cell.

In certain embodiments, combinatorial libraries of potential modulators will be screened for an ability to bind to a prostate cancer polypeptide or to modulate activity. Conventionally, new chemical entities with useful properties are generated by identifying a chemical compound (called a "lead compound") with some desirable property or activity, e.g., inhibiting activity, creating variants of the lead compound, and evaluating the property and activity of those variant compounds. Often, high throughput screening (HTS) methods are employed for such an analysis.

In one preferred embodiment, high throughput screening methods involve providing a library containing a large number of potential therapeutic compounds (candidate

compounds). Such "combinatorial chemical libraries" are then screened in one or more assays to identify those library members (particular chemical species or subclasses) that display a desired characteristic activity. The compounds thus identified can serve as conventional "lead compounds" or can themselves be used as potential or actual therapeutics.

5 A combinatorial chemical library is a collection of diverse chemical compounds generated by either chemical synthesis or biological synthesis by combining a number of chemical "building blocks" such as reagents. For example, a linear combinatorial chemical library, such as a polypeptide (e.g., mutein) library, is formed by combining a set of chemical building blocks called amino acids in most every possible way for a given compound length
10 (i.e., the number of amino acids in a polypeptide compound). Millions of chemical compounds can be synthesized through such combinatorial mixing of chemical building blocks. Gallop, et al. (1994) J. Med. Chem. 37:1233-1251.

Preparation and screening of combinatorial chemical libraries is well known to those of skill in the art. Such combinatorial chemical libraries include, but are not limited to,
15 peptide libraries (see, e.g., U.S. Patent No. 5,010,175, Furka (1991) Pept. Prot. Res. 37:487-493, Houghton, et al. (1991) Nature, 354:84-88), peptoids (PCT Publication No WO 91/19735), encoded peptides (PCT Publication WO 93/20242), random bio-oligomers (PCT Publication WO 92/00091), benzodiazepines (U.S. Pat. No. 5,288,514), diversomers such as hydantoins, benzodiazepines and dipeptides (Hobbs, et al. (1993) Proc. Nat. Acad. Sci. USA
20 90:6909-6913), vinylogous polypeptides (Hagihara, et al. (1992) J. Amer. Chem. Soc. 114:6568-xxx), nonpeptidal peptidomimetics with a Beta-D-Glucose scaffolding (Hirschmann, et al. (1992) J. Amer. Chem. Soc. 114:9217-9218), analogous organic syntheses of small compound libraries (Chen, et al. (1994) J. Amer. Chem. Soc. 116:2661-xxx), oligocarbamates (Cho, et al. (1993) Science 261:1303-1305), and/or peptidyl
25 phosphonates (Campbell, et al. (1994) J. Org. Chem. 59:658-xxx). See, generally, Gordon, et al. (1994) J. Med. Chem. 37:1385-1401), nucleic acid libraries (see, e.g., Stratagene, Corp.), peptide nucleic acid libraries (see, e.g., U.S. Patent 5,539,083), antibody libraries (see, e.g., Vaughn, et al. (1996) Nature Biotechnology 14:309-314, and PCT/US96/10287), carbohydrate libraries (see, e.g., Liang, et al. (1996) Science 274:1520-1522, and U.S. Patent
30 No. 5,593,853), and small organic molecule libraries (see, e.g., benzodiazepines, Baum (1993) C&EN, Jan 18, page 33; isoprenoids, U.S. Patent No. 5,569,588; thiazolidinones and metathiazanones, U.S. Patent No. 5,549,974; pyrrolidines, U.S. Patent Nos. 5,525,735 and

5,519,134; morpholino compounds, U.S. Patent No. 5,506,337; benzodiazepines, U.S. Patent No. 5,288,514; and the like).

Devices for the preparation of combinatorial libraries are commercially available (see, e.g., 357 MPS, 390 MPS, Advanced Chem Tech, Louisville KY, Symphony, Rainin,

- 5 Woburn, MA, 433A Applied Biosystems, Foster City, CA, 9050 Plus, Millipore, Bedford, MA).

A number of well known robotic systems have also been developed for solution phase chemistries. These systems include automated workstations like the automated synthesis apparatus developed by Takeda Chemical Industries, LTD. (Osaka, Japan) and many robotic systems utilizing robotic arms (Zymate II, Zymark Corporation, Hopkinton, Mass.; Orca, Hewlett-Packard, Palo Alto, Calif.), which mimic the manual synthetic operations performed by a chemist. Many of the above devices are suitable for use with the present invention. The nature and implementation of modifications to these devices (if any) so that they can operate as discussed herein will be apparent to persons skilled in the relevant art. In addition,

- 15 numerous combinatorial libraries are themselves commercially available (see, e.g., ComGenex, Princeton, N.J., Asinex, Moscow, Ru, Tripos, Inc., St. Louis, MO, ChemStar, Ltd, Moscow, RU, 3D Pharmaceuticals, Exton, PA, Martek Biosciences, Columbia, MD, etc.).

The assays to identify modulators are amenable to high throughput screening.

- 20 Preferred assays thus detect enhancement or inhibition of prostate cancer gene transcription, inhibition or enhancement of polypeptide expression, and inhibition or enhancement of polypeptide activity.

High throughput assays for the presence, absence, quantification, or other properties of particular nucleic acids or protein products are well known to those of skill in the art.

- 25 Similarly, binding assays and reporter gene assays are similarly well known. Thus, e.g., U.S. Patent No. 5,559,410 discloses high throughput screening methods for proteins, U.S. Patent No. 5,585,639 discloses high throughput screening methods for nucleic acid binding (i.e., in arrays), while U.S. Patent Nos. 5,576,220 and 5,541,061 disclose high throughput methods of screening for ligand/antibody binding.

- 30 In addition, high throughput screening systems are commercially available (see, e.g., Zymark Corp., Hopkinton, MA; Air Technical Industries, Mentor, OH; Beckman Instruments, Inc. Fullerton, CA; Precision Systems, Inc., Natick, MA, etc.). These systems

typically automate entire procedures, including sample and reagent pipetting, liquid dispensing, timed incubations, and final readings of the microplate in detector(s) appropriate for the assay. These configurable systems provide high throughput and rapid start up as well as a high degree of flexibility and customization. The manufacturers of such systems provide
5 detailed protocols for various high throughput systems. Thus, e.g., Zymark Corp. provides technical bulletins describing screening systems for detecting the modulation of gene transcription, ligand binding, and the like.

In one embodiment, modulators are proteins, often naturally occurring proteins or fragments of naturally occurring proteins. Thus, e.g., cellular extracts containing proteins, or
10 random or directed digests of proteinaceous cellular extracts, may be used. In this way libraries of proteins may be made for screening in the methods of the invention. Particularly preferred in this embodiment are libraries of bacterial, fungal, viral, and mammalian proteins, with the latter being preferred, and human proteins being especially preferred. Particularly useful test compound will be directed to the class of proteins to which the target belongs, e.g.,
15 substrates for enzymes or ligands and receptors.

In a preferred embodiment, modulators are peptides of from about 5 to about 30 amino acids, with from about 5 to about 20 amino acids being preferred, and from about 7 to about 15 being particularly preferred. The peptides may be digests of naturally occurring proteins as is outlined above, random peptides, or "biased" random peptides. By
20 "randomized" or grammatical equivalents herein is meant that each nucleic acid and peptide consists of essentially random nucleotides and amino acids, respectively. Since generally these random peptides (or nucleic acids, discussed below) are chemically synthesized, they may typically incorporate any nucleotide or amino acid at any position. The synthetic process can be designed to generate randomized proteins or nucleic acids, to allow the
25 formation of all or most of the possible combinations over the length of the sequence, thus forming a library of randomized candidate bioactive proteinaceous agents.

In one embodiment, the library is fully randomized, with no sequence preferences or constants at any position. In a preferred embodiment, the library is biased. That is, some positions within the sequence are either held constant, or are selected from a limited number
30 of possibilities. For example, in a preferred embodiment, the nucleotides or amino acid residues are randomized within a defined class, e.g., of hydrophobic amino acids, hydrophilic residues, sterically biased (either small or large) residues, towards the creation of nucleic acid

binding domains, the creation of cysteines, for cross-linking, prolines for SH-3 domains, serines, threonines, tyrosines, or histidines for phosphorylation sites, etc., or to purines, etc.

Modulators of prostate cancer can also be nucleic acids, as defined above.

As described above generally for proteins, nucleic acid modulating agents may be
5 naturally occurring nucleic acids, random nucleic acids, or "biased" random nucleic acids. For example, digests of prokaryotic or eukaryotic genomes may be used as is outlined above for proteins.

In a preferred embodiment, the candidate compounds are organic chemical moieties, a wide variety of which are available in the literature.

10 After the candidate agent has been added and the cells allowed to incubate for some period of time, the sample containing a target sequence to be analyzed is added to the biochip. If required, the target sequence is prepared using known techniques. For example, the sample may be treated to lyse the cells, using known lysis buffers, electroporation, etc., with purification and/or amplification such as PCR performed as appropriate. For example,
15 an in vitro transcription with labels covalently attached to the nucleotides is performed. Generally, the nucleic acids are labeled with biotin-FITC or PE, or with cy3 or cy5.

In a preferred embodiment, the target sequence is labeled with, e.g., a fluorescent, a chemiluminescent, a chemical, or a radioactive signal, to provide a means of detecting the target sequence's specific binding to a probe. The label also can be an enzyme, such as,
20 alkaline phosphatase or horseradish peroxidase, which when provided with an appropriate substrate produces a product that can be detected. Alternatively, the label can be a labeled compound or small molecule, such as an enzyme inhibitor, that binds but is not catalyzed or altered by the enzyme. The label also can be a moiety or compound, such as, an epitope tag or biotin which specifically binds to streptavidin. For the example of biotin, the streptavidin
25 is labeled as described above, thereby, providing a detectable signal for the bound target sequence. Unbound labeled streptavidin is typically removed prior to analysis.

As will be appreciated by those in the art, these assays can be direct hybridization assays or can comprise "sandwich assays", which include the use of multiple probes, as is generally outlined in U.S. Patent Nos. 5,681,702, 5,597,909, 5,545,730, 5,594,117,
30 5,591,584, 5,571,670, 5,580,731, 5,571,670, 5,591,584, 5,624,802, 5,635,352, 5,594,118, 5,359,100, 5,124,246, and 5,681,697, each of which is hereby incorporated by reference. In this embodiment, in general, the target nucleic acid is prepared as outlined above, and then

added to the biochip comprising a plurality of nucleic acid probes, under conditions that allow the formation of a hybridization complex.

A variety of hybridization conditions may be used in the present invention, including high, moderate, and low stringency conditions as outlined above. The assays are generally run under stringency conditions which allows formation of the label probe hybridization complex only in the presence of target. Stringency can be controlled by altering a step parameter that is a thermodynamic variable, including, but not limited to, temperature, formamide concentration, salt concentration, chaotropic salt concentration pH, organic solvent concentration, etc.

These parameters may also be used to control non-specific binding, as is generally outlined in U.S. Patent No. 5,681,697. Thus it may be desirable to perform certain steps at higher stringency conditions to reduce non-specific binding.

The reactions outlined herein may be accomplished in a variety of ways. Components of the reaction may be added simultaneously, or sequentially, in different orders, with preferred embodiments outlined below. In addition, the reaction may include a variety of other reagents. These include salts, buffers, neutral proteins, e.g., albumin, detergents, etc., which may be used to facilitate optimal hybridization and detection, and/or reduce non-specific or background interactions. Reagents that otherwise improve the efficiency of the assay, such as protease inhibitors, nuclease inhibitors, anti-microbial agents, etc., may also be used as appropriate, depending on the sample preparation methods and purity of the target.

The assay data are analyzed to determine the expression levels, and changes in expression levels as between states, of individual genes, forming a gene expression profile.

Screens are performed to identify modulators of the prostate cancer or related phenotype. In one embodiment, screening is performed to identify modulators that can induce or suppress a particular expression profile, thus preferably generating the associated phenotype. In another embodiment, e.g., for diagnostic applications, having identified differentially expressed genes important in a particular state, screens can be performed to identify modulators that alter expression of individual genes. In an another embodiment, screening is performed to identify modulators that alter a biological function of the expression product of a differentially expressed gene. Again, having identified the importance of a gene in a particular state, screens are performed to identify agents that bind and/or modulate the biological activity of the gene product.

In addition screens can be done for genes that are induced in response to a candidate agent. After identifying a modulator based upon its ability to suppress a prostate cancer expression pattern leading to a normal expression pattern, or to modulate a single prostate cancer gene expression profile so as to mimic the expression of the gene from normal tissue, a screen as described above can be performed to identify genes that are specifically modulated in response to the agent. Comparing expression profiles between normal tissue and agent treated prostate cancer tissue reveals genes that are not expressed in normal tissue or prostate cancer tissue, but are expressed in agent treated tissue. These agent-specific sequences can be identified and used by methods described herein for prostate cancer genes or proteins. In particular these sequences and the proteins they encode find use in marking or identifying agent treated cells. In addition, antibodies can be raised against the agent induced proteins and used to target novel therapeutics to the treated prostate cancer tissue sample.

Thus, in one embodiment, a test compound is administered to a population of prostate cancer cells, that have an associated prostate cancer expression profile. By "administration" or "contacting" herein is meant that the candidate agent is added to the cells in such a manner as to allow the agent to act upon the cell, whether by uptake and intracellular action, or by action at the cell surface. In some embodiments, nucleic acid encoding a proteinaceous candidate agent (e.g., a peptide) may be put into a viral construct such as an adenoviral or retroviral construct, and added to the cell, such that expression of the peptide agent is accomplished, e.g., PCT US97/01019. Regulatable gene therapy systems can also be used.

Once the test compound has been administered to the cells, the cells can be washed if desired and are allowed to incubate under preferably physiological conditions for some period of time. The cells are then harvested and a new gene expression profile is generated, as outlined herein.

Thus, e.g., prostate cancer or non-malignant tissue may be screened for agents that modulate, e.g., induce or suppress the prostate cancer or related phenotype. A change in at least one gene, preferably many, of the expression profile indicates that the agent has an effect on prostate cancer activity. By defining such a signature for the prostate cancer phenotype, screens for new drugs that alter the phenotype can be devised. With this approach, the drug target need not be known and need not be represented in the original expression screening platform, nor does the level of transcript for the target protein need to change.

In a preferred embodiment, as outlined above, screens may be done on individual genes and gene products (proteins). That is, having identified a particular differentially expressed gene as important in a particular state, screening of modulators of either the expression of the gene or the gene product itself can be done. The gene products of differentially expressed genes are sometimes referred to herein as "prostate cancer proteins" or a "prostate cancer modulatory protein". The prostate cancer modulatory protein may be a fragment, or alternatively, be the full length protein to the fragment encoded by the nucleic acids of the Tables 1A-4. Preferably, the prostate cancer modulatory protein is a fragment. In a preferred embodiment, the prostate cancer amino acid sequence which is used to determine sequence identity or similarity is encoded by a nucleic acid of Tables 1A-4. In another embodiment, the sequences are naturally occurring allelic variants of a protein encoded by a nucleic acid of Tables 1A-4. In another embodiment, the sequences are sequence variants as further described herein.

Preferably, the prostate cancer modulatory protein is a fragment of approximately 14 to 24 amino acids long. More preferably the fragment is a soluble fragment. Preferably, the fragment includes a non-transmembrane region. In a preferred embodiment, the fragment has an N-terminal Cys to aid in solubility. In one embodiment, the C-terminus of the fragment is kept as a free acid and the N-terminus is a free amine to aid in coupling, i.e., to cysteine.

In one embodiment the prostate cancer proteins are conjugated to an immunogenic agent as discussed herein. In one embodiment the prostate cancer protein is conjugated to BSA.

Measurements of prostate cancer polypeptide activity, or of prostate cancer or the prostate cancer phenotype can be performed using a variety of assays. For example, the effects of the test compounds upon the function of the prostate cancer polypeptides can be measured by examining parameters described above. A suitable physiological change that affects activity can be used to assess the influence of a test compound on the polypeptides of this invention. When the functional consequences are determined using intact cells or animals, one can also measure a variety of effects such as, in the case of prostate cancer associated with tumors, tumor growth, tumor metastasis, neovascularization, hormone release, transcriptional changes to both known and uncharacterized genetic markers (e.g., northern blots), changes in cell metabolism such as cell growth or pH changes, and changes

in intracellular second messengers such as cGMP. In the assays of the invention, a mammalian prostate cancer polypeptide is typically used, e.g., mouse, preferably human.

Assays to identify compounds with modulating activity can be performed in vitro. For example, a prostate cancer polypeptide is first contacted with a potential modulator and incubated for a suitable amount of time, e.g., from 0.5 to 48 hours. In one embodiment, the prostate cancer polypeptide levels are determined in vitro by measuring the level of protein or mRNA. The level of protein is measured using immunoassays such as western blotting, ELISA, and the like with an antibody that selectively binds to the prostate cancer polypeptide or a fragment thereof. For measurement of mRNA, amplification, e.g., using PCR, LCR, or hybridization assays, e.g., northern hybridization, RNase protection, dot blotting, are preferred. The level of protein or mRNA is detected using directly or indirectly labeled detection agents, e.g., fluorescently or radioactively labeled nucleic acids, radioactively or enzymatically labeled antibodies, and the like, as described herein.

Alternatively, a reporter gene system can be devised using the prostate cancer protein promoter operably linked to a reporter gene such as luciferase, green fluorescent protein, CAT, or β -gal. The reporter construct is typically transfected into a cell. After treatment with a potential modulator, the amount of reporter gene transcription, translation, or activity is measured according to standard techniques known to those of skill in the art.

In a preferred embodiment, as outlined above, screens may be done on individual genes and gene products (proteins). That is, having identified a particular differentially expressed gene as important in a particular state, screening of modulators of the expression of the gene or the gene product itself can be done. The gene products of differentially expressed genes are sometimes referred to herein as "prostate cancer proteins." The prostate cancer protein may be a fragment, or alternatively, be the full length protein corresponding to a fragment shown herein.

In one embodiment, screening for modulators of expression of specific genes is performed. Typically, the expression of only one or a few genes are evaluated. In another embodiment, screens are designed to first find compounds that bind to differentially expressed proteins. These compounds are then evaluated for the ability to modulate differentially expressed activity. Moreover, once initial candidate compounds are identified, variants can be further screened to better evaluate structure activity relationships.

In a preferred embodiment, binding assays are done. In general, purified or isolated gene product is used; that is, the gene products of one or more differentially expressed nucleic acids are made. For example, antibodies are generated to the protein gene products, and standard immunoassays are run to determine the amount of protein present.

5 Alternatively, cells comprising the prostate cancer proteins can be used in the assays.

Thus, in a preferred embodiment, the methods comprise combining a prostate cancer protein and a candidate compound, and determining the binding of the compound to the prostate cancer protein. Preferred embodiments utilize the human prostate cancer protein, although other mammalian proteins may also be used, e.g., for the development of animal
10 models of human disease. In some embodiments, as outlined herein, variant or derivative prostate cancer proteins may be used.

Generally, in a preferred embodiment of the methods herein, the prostate cancer protein or the candidate agent is non-diffusably bound to an insoluble support having isolated sample receiving areas (e.g., a microtiter plate, an array, etc.). The insoluble supports may be
15 made of a composition to which the compositions can be bound, is readily separated from soluble material, and is otherwise compatible with the overall method of screening. The surface of such supports may be solid or porous and of a convenient shape. Examples of suitable insoluble supports include microtiter plates, arrays, membranes, and beads. These are typically made of glass, plastic (e.g., polystyrene), polysaccharides, nylon or
20 nitrocellulose, teflon™, etc. Microtiter plates and arrays are especially convenient because a large number of assays can be carried out simultaneously, using small amounts of reagents and samples. The particular manner of binding of the composition should be compatible with the reagents and overall methods of the invention, maintain the activity of the composition, and be nondiffusable. Preferred methods of binding include the use of antibodies (which do
25 not sterically block either the ligand binding site or activation sequence when the protein is bound to the support), direct binding to "sticky" or ionic supports, chemical crosslinking, the synthesis of the protein or agent on the surface, etc. Following binding of the protein or agent, excess unbound material is removed by washing. The sample receiving areas may then be blocked through incubation with bovine serum albumin (BSA), casein, or other
30 innocuous protein or other moiety.

In a preferred embodiment, the prostate cancer protein is bound to the support, and a test compound is added to the assay. Alternatively, the candidate agent is bound to the

support and the prostate cancer protein is added. Novel binding agents include specific antibodies, non-natural binding agents identified in screens of chemical libraries, peptide analogs, etc. Of particular interest are screening assays for agents that have a low toxicity for human cells. A wide variety of assays may be used for this purpose, including labeled in vitro protein-protein binding assays, electrophoretic mobility shift assays, immunoassays for protein binding, functional assays (phosphorylation assays, etc.) and the like.

The determination of the binding of the test modulating compound to the prostate cancer protein may be done in a number of ways. In a preferred embodiment, the compound is labeled, and binding determined directly, e.g., by attaching all or a portion of the prostate cancer protein to a solid support, adding a labeled candidate agent (e.g., a fluorescent label), washing off excess reagent, and determining whether the label is present on the solid support. Various blocking and washing steps may be utilized as appropriate.

In some embodiments, only one of the components is labeled, e.g., the proteins (or proteinaceous candidate compounds) can be labeled. Alternatively, more than one component can be labeled with different labels, e.g., ^{125}I for the proteins and a fluorophor for the compound. Proximity reagents, e.g., quenching or energy transfer reagents are also useful.

In one embodiment, the binding of the test compound is determined by competitive binding assay. The competitor is a binding moiety known to bind to the target molecule (i.e., a prostate cancer protein), such as an antibody, peptide, binding partner, ligand, etc. Under certain circumstances, there may be competitive binding between the compound and the binding moiety, with the binding moiety displacing the compound. In one embodiment, the test compound is labeled. Either the compound, or the competitor, or both, is added first to the protein for a time sufficient to allow binding, if present. Incubations may be performed at a temperature which facilitates optimal activity, typically between 4 and 40° C. Incubation periods are typically optimized, e.g., to facilitate rapid high throughput screening. Typically between 0.1 and 1 hour will be sufficient. Excess reagent is generally removed or washed away. The second component is then added, and the presence or absence of the labeled component is followed, to indicate binding.

In a preferred embodiment, the competitor is added first, followed by the test compound. Displacement of the competitor is an indication that the test compound is binding to the prostate cancer protein and thus is capable of binding to, and potentially modulating,

the activity of the prostate cancer protein. In this embodiment, either component can be labeled. Thus, e.g., if the competitor is labeled, the presence of label in the wash solution indicates displacement by the agent. Alternatively, if the test compound is labeled, the presence of the label on the support indicates displacement.

5 In an alternative embodiment, the test compound is added first, with incubation and washing, followed by the competitor. The absence of binding by the competitor may indicate that the test compound is bound to the prostate cancer protein with a higher affinity. Thus, if the test compound is labeled, the presence of the label on the support, coupled with a lack of competitor binding, may indicate that the test compound is capable of binding to the prostate cancer protein.

10 In a preferred embodiment, the methods comprise differential screening to identify agents that are capable of modulating the activity of the prostate cancer proteins. In this embodiment, the methods comprise combining a prostate cancer protein and a competitor in a first sample. A second sample comprises a test compound, a prostate cancer protein, and a competitor. The binding of the competitor is determined for both samples, and a change, or difference in binding between the two samples indicates the presence of an agent capable of binding to the prostate cancer protein and potentially modulating its activity. That is, if the binding of the competitor is different in the second sample relative to the first sample, the agent is capable of binding to the prostate cancer protein.

20 Alternatively, differential screening is used to identify drug candidates that bind to the native prostate cancer protein, but cannot bind to modified prostate cancer proteins. The structure of the prostate cancer protein may be modeled, and used in rational drug design to synthesize agents that interact with that site. Drug candidates that affect the activity of a prostate cancer protein are also identified by screening drugs for the ability to either enhance or reduce the activity of the protein.

25 Positive controls and negative controls may be used in the assays. Preferably control and test samples are performed in at least triplicate to obtain statistically significant results. Incubation of samples is for a time sufficient for the binding of the agent to the protein. Following incubation, samples are washed free of non-specifically bound material and the amount of bound, generally labeled agent determined. For example, where a radiolabel is employed, the samples may be counted in a scintillation counter to determine the amount of bound compound.

A variety of other reagents may be included in the screening assays. These include reagents like salts, neutral proteins, e.g., albumin, detergents, etc., which may be used to facilitate optimal protein-protein binding and/or reduce non-specific or background interactions. Also reagents that otherwise improve the efficiency of the assay, such as protease inhibitors, nuclease inhibitors, anti-microbial agents, etc., may be used. The mixture of components may be added in an order that provides for the requisite binding.

In a preferred embodiment, the invention provides methods for screening for a compound capable of modulating the activity of a prostate cancer protein. The methods comprise adding a test compound, as defined above, to a cell comprising prostate cancer proteins. Preferred cell types include almost any cell. The cells contain a recombinant nucleic acid that encodes a prostate cancer protein. In a preferred embodiment, a library of candidate agents are tested on a plurality of cells.

In one aspect, the assays are evaluated in the presence or absence or previous or subsequent exposure of physiological signals, e.g., hormones, antibodies, peptides, antigens, cytokines, growth factors, action potentials, pharmacological agents including chemotherapeutics, radiation, carcinogenics, or other cells (e.g., cell-cell contacts). In another example, the determinations are determined at different stages of the cell cycle process.

In this way, compounds that modulate prostate cancer agents are identified. Compounds with pharmacological activity are able to enhance or interfere with the activity of the prostate cancer protein. Once identified, similar structures are evaluated to identify critical structural feature of the compound.

In one embodiment, a method of inhibiting prostate cancer cell division is provided. The method comprises administration of a prostate cancer inhibitor. In another embodiment, a method of inhibiting prostate cancer or other prostate proliferative condition is provided. The method comprises administration of a prostate cancer inhibitor. In a further embodiment, methods of treating cells or individuals with prostate cancer are provided. The method comprises administration of a prostate cancer inhibitor.

In one embodiment, a prostate cancer inhibitor is an antibody as discussed above. In another embodiment, the prostate cancer inhibitor is an antisense molecule.

A variety of cell growth, proliferation, and metastasis assays are known to those of skill in the art, as described below.

Soft agar growth or colony formation in suspension

Normal cells require a solid substrate to attach and grow. When the cells are transformed, they lose this phenotype and grow detached from the substrate. For example, transformed cells can grow in stirred suspension culture or suspended in semi-solid media, such as semi-solid or soft agar. The transformed cells, when transfected with tumor suppressor genes, regenerate normal phenotype and require a solid substrate to attach and grow. Soft agar growth or colony formation in suspension assays can be used to identify modulators of prostate cancer sequences, which when expressed in host cells, inhibit abnormal cellular proliferation and transformation. A therapeutic compound would reduce or eliminate the host cells' ability to grow in stirred suspension culture or suspended in semi-solid media, such as semi-solid or soft.

Techniques for soft agar growth or colony formation in suspension assays are described in Freshney (1994) Culture of Animal Cells a Manual of Basic Technique 3d ed. Wiley-Liss, herein incorporated by reference. See also, the methods section of Garkavtsev, et al. (1996), supra, herein incorporated by reference.

Contact inhibition and density limitation of growth

Normal cells typically grow in a flat and organized pattern in a petri dish until they touch other cells. When the cells touch one another, they are contact inhibited and stop growing. When cells are transformed, however, the cells are not contact inhibited and continue to grow to high densities in disorganized foci. Thus, the transformed cells grow to a higher saturation density than normal cells. This can be detected morphologically by the formation of a disoriented monolayer of cells or rounded cells in foci within the regular pattern of normal surrounding cells. Alternatively, labeling index with (^3H)-thymidine at saturation density can be used to measure density limitation of growth. See Freshney (1994), supra. The transformed cells, when transfected with tumor suppressor genes, regenerate a normal phenotype and become contact inhibited and would grow to a lower density.

In this assay, labeling index with (^3H)-thymidine at saturation density is a preferred method of measuring density limitation of growth. Transformed host cells are transfected with a prostate cancer-associated sequence and are grown for 24 hours at saturation density in non-limiting medium conditions. The percentage of cells labeling with (^3H)-thymidine is determined autoradiographically. See, Freshney (1994), supra.

Growth factor or serum dependence

Transformed cells have a lower serum dependence than their normal counterparts (see, e.g., Temin (1966) J. Natl. Cancer Inst. 37:167-175; Eagle, et al. (1970) J. Exp. Med. 131:836-879); Freshney, supra. This is in part due to release of various growth factors by the transformed cells. Growth factor or serum dependence of transformed host cells can be compared with that of control.

Tumor specific markers levels

Tumor cells release an increased amount of certain factors (hereinafter "tumor specific markers") than their normal counterparts. For example, plasminogen activator (PA) is released from human glioma at a higher level than from normal brain cells (see, e.g., Gullino, "Angiogenesis, tumor vascularization, and potential interference with tumor growth" pp. 178-184 in Mihich (ed. 1985) Biological Responses in Cancer Plenum. Similarly, Tumor angiogenesis factor (TAF) is released at a higher level in tumor cells than their normal counterparts. See, e.g., Folkman (1992) Angiogenesis and Cancer, Sem. Cancer Biol.

Various techniques which measure the release of these factors are described in Freshney (1994), supra. Also, see, Unkless, et al. (1974) J. Biol. Chem. 249:4295-4305; Strickland and Beers (1976) J. Biol. Chem. 251:5694-5702; Whur, et al. (1980) Br. J. Cancer 42:305-312; Gullino, "Angiogenesis, tumor vascularization, and potential interference with tumor growth" pp. 178-184 in Mihich (ed. 1985) Biological Responses in Cancer Plenum; and Freshney (1985) Anticancer Res. 5:111-130.

Invasiveness into Matrigel

The degree of invasiveness into Matrigel or some other extracellular matrix constituent can be used as an assay to identify compounds that modulate prostate cancer-associated sequences. Tumor cells exhibit a good correlation between malignancy and invasiveness of cells into Matrigel or some other extracellular matrix constituent. In this assay, tumorigenic cells are typically used as host cells. Expression of a tumor suppressor gene in these host cells would decrease invasiveness of the host cells.

Techniques described in Freshney (1994), supra, can be used. Briefly, the level of invasion of host cells can be measured by using filters coated with Matrigel or some other extracellular matrix constituent. Penetration into the gel, or through to the distal side of the filter, is rated as invasiveness, and rated histologically by number of cells and distance moved, or by prelabeling the cells with ¹²⁵I and counting the radioactivity on the distal side of the filter or bottom of the dish. See, e.g., Freshney (1984), supra.

Tumor growth in vivo

Effects of prostate cancer-associated sequences on cell growth can be tested in transgenic or immune-suppressed mice. Knock-out transgenic mice can be made, in which the prostate cancer gene is disrupted or in which a prostate cancer gene is inserted. Knock-out transgenic mice can be made by insertion of a marker gene or other heterologous gene into the endogenous prostate cancer gene site in the mouse genome via homologous recombination. Such mice can also be made by substituting the endogenous prostate cancer gene with a mutated version of the prostate cancer gene, or by mutating the endogenous prostate cancer gene, e.g., by exposure to carcinogens.

A DNA construct is introduced into the nuclei of embryonic stem cells. Cells containing the newly engineered genetic lesion are injected into a host mouse embryo, which is re-implanted into a recipient female. Some of these embryos develop into chimeric mice that possess germ cells partially derived from the mutant cell line. Therefore, by breeding the chimeric mice it is possible to obtain a new line of mice containing the introduced genetic lesion (see, e.g., Capecchi, et al. (1989) Science 244:1288-1292). Chimeric targeted mice can be derived according to Hogan, et al. (1988) Manipulating the Mouse Embryo: A Laboratory Manual CSH Press; and Robertson (ed. 1987) Teratocarcinomas and Embryonic Stem Cells: A Practical Approach IRL Press, Washington, D.C.

Alternatively, various immune-suppressed or immune-deficient host animals can be used. For example, genetically athymic "nude" mouse (see, e.g., Giovanella, et al. (1974) J. Natl. Cancer Inst. 52:921-930), a SCID mouse, a thymectomized mouse, or an irradiated mouse (see, e.g., Bradley, et al. (1978) Br. J. Cancer 38:263-272; Selby, et al. (1980) Br. J. Cancer 41:52-61) can be used as a host. Transplantable tumor cells (typically about 10^5 cells) injected into isogenic hosts will produce invasive tumors in a high proportions of cases, while normal cells of similar origin will not. In hosts which developed invasive tumors, cells expressing a prostate cancer-associated sequences are injected subcutaneously. After a suitable length of time, preferably 4-8 weeks, tumor growth is measured (e.g., by volume or by its two largest dimensions) and compared to the control. Tumors that have statistically significant reduction (using, e.g., Student's T test) are said to have inhibited growth.

Polynucleotide modulators of prostate cancer

Antisense and RNAi Polynucleotides

In certain embodiments, the activity of a prostate cancer-associated protein is down-regulated, or entirely inhibited, by the use of antisense polynucleotide, i.e., a nucleic acid complementary to, and which can preferably hybridize specifically to, a coding mRNA nucleic acid sequence, e.g., a prostate cancer protein mRNA, or a subsequence thereof.

- 5 Binding of the antisense polynucleotide to the mRNA reduces the translation and/or stability of the mRNA.

In the context of this invention, antisense polynucleotides can comprise naturally-occurring nucleotides, or synthetic species formed from naturally-occurring subunits or their close homologs. Antisense polynucleotides may also have altered sugar moieties or inter-sugar linkages. Exemplary among these are the phosphorothioate and other sulfur containing species which are known for use in the art. Analogs are comprehended by this invention so long as they function effectively to hybridize with the prostate cancer protein mRNA. See, e.g., Isis Pharmaceuticals, Carlsbad, CA; Sequitor, Inc., Natick, MA.

- 15 Such antisense polynucleotides can readily be synthesized using recombinant means, or can be synthesized in vitro. Equipment for such synthesis is sold by several vendors, including Applied Biosystems. The preparation of other oligonucleotides such as phosphorothioates and alkylated derivatives is also well known to those of skill in the art.

Antisense molecules as used herein include antisense or sense oligonucleotides. Sense oligonucleotides can, e.g., be employed to block transcription by binding to the anti-sense strand. The antisense and sense oligonucleotide comprise a single-stranded nucleic acid sequence (either RNA or DNA) capable of binding to target mRNA (sense) or DNA (antisense) sequences for prostate cancer molecules. A preferred antisense molecule is for a prostate cancer sequences in Tables 1A-4, or for a ligand or activator thereof. Antisense or sense oligonucleotides, according to the present invention, comprise a fragment generally at least about 14 nucleotides, preferably from about 14 to 30 nucleotides. The ability to derive an antisense or a sense oligonucleotide, based upon a cDNA sequence encoding a given protein is described in, e.g., Stein and Cohen (1988) Cancer Res. 48:2659-2668; and van der Krol, et al. (1988) BioTechniques 6:958-976.

- 30 RNA interference is a mechanism to suppress gene expression in a sequence specific manner. See, e.g., Brumelkamp, et al. (2002) Scienceexpress (21March2002); Sharp (1999) Genes Dev. 13:139-141; and Cathew (2001) Curr. Op. Cell Biol. 13:244-248. In mammalian cells, short, e.g., 21 nt, double stranded small interfering RNAs (siRNA) have been shown to

be effective at inducing an RNAi response. See, e.g., Elbashir, et al. (2001) Nature 411:494-498. The mechanism may be used to downregulate expression levels of identified genes, e.g., treatment of or validation of relevance to disease.

5 Ribozymes

In addition to antisense polynucleotides, ribozymes can be used to target and inhibit transcription of prostate cancer-associated nucleotide sequences. A ribozyme is an RNA molecule that catalytically cleaves other RNA molecules. Different kinds of ribozymes have been described, including group I ribozymes, hammerhead ribozymes, hairpin ribozymes, RNase P, and axhead ribozymes (see, e.g., Castanotto, et al. (1994) Adv. in Pharmacology 25: 289-317 for a general review of the properties of different ribozymes).

The general features of hairpin ribozymes are described, e.g., in Hampel, et al. (1990) Nucl. Acids Res. 18:299-304; European Patent Publication No. 0 360 257; U.S. Patent No. 5,254,678. Methods of preparing are well known to those of skill in the art. See, e.g., WO 94/26877; Ojwang, et al. (1993) Proc. Natl. Acad. Sci. USA 90:6340-6344; Yamada, et al. (1994) Human Gene Therapy 1:39-45; Leavitt, et al. (1995) Proc. Natl. Acad. Sci. USA 92:699-703; Leavitt, et al. (1994) Human Gene Therapy 5:1151-120; and Yamada, et al. (1994) Virology 205:121-126.

Polynucleotide modulators of prostate cancer may be introduced into a cell containing the target nucleotide sequence by formation of a conjugate with a ligand binding molecule, as described in WO 91/04753. Suitable ligand binding molecules include, but are not limited to, cell surface receptors, growth factors, other cytokines, or other ligands that bind to cell surface receptors. Preferably, conjugation of the ligand binding molecule does not substantially interfere with the ability of the ligand binding molecule to bind to its corresponding molecule or receptor, or block entry of the sense or antisense oligonucleotide or its conjugated version into the cell. Alternatively, a polynucleotide modulator of prostate cancer may be introduced into a cell containing the target nucleic acid sequence, e.g., by formation of an polynucleotide-lipid complex, as described in WO 90/10448. It is understood that the use of antisense molecules or knock out and knock in models may also be used in screening assays as discussed above, in addition to methods of treatment.

Thus, in one embodiment, methods of modulating prostate disorders, e.g., cancer in cells or organisms, are provided. In one embodiment, the methods comprise administering to

a patient, e.g., to a cell within the patient, an anti-prostate cancer antibody that reduces or eliminates the biological activity of an endogenous prostate cancer protein. Alternatively, the methods comprise administering to a cell or organism a recombinant nucleic acid encoding a prostate cancer protein. This may be accomplished in many ways. In a preferred
5 embodiment, e.g., when the prostate cancer sequence is down-regulated in prostate cancer, such state may be reversed by increasing the amount of prostate cancer gene product in the cell. This can be accomplished, e.g., by overexpressing the endogenous prostate cancer gene or administering a gene encoding the prostate cancer sequence, using known gene-therapy techniques, e.g.. In a preferred embodiment, the gene therapy techniques include the
10 incorporation of the exogenous gene using enhanced homologous recombination (EHR), e.g., as described in PCT/US93/03868, hereby incorporated by reference in its entirety. Alternatively, e.g., when the prostate cancer sequence is up-regulated in prostate cancer, the activity of the endogenous prostate cancer gene is decreased, e.g., by the administration of a prostate cancer antisense nucleic acid.

15 In one embodiment, the prostate cancer proteins of the present invention may be used to generate polyclonal and monoclonal antibodies to prostate cancer proteins. Similarly, the prostate cancer proteins can be coupled, using standard technology, to affinity chromatography columns. These columns may then be used to purify prostate cancer antibodies useful for production, diagnostic, or therapeutic purposes. In a preferred
20 embodiment, the antibodies are generated to epitopes unique to a prostate cancer protein; that is, the antibodies show little or no cross-reactivity to other proteins. The prostate cancer antibodies may be coupled to standard affinity chromatography columns and used to purify prostate cancer proteins. The antibodies may also be used as blocking polypeptides, as outlined above, since they will specifically bind to the prostate cancer protein.

25

Methods of identifying variant prostate cancer-associated sequences

Without being bound by theory, expression of various prostate cancer sequences is correlated with prostate cancer or other prostate disorders. Accordingly, disorders based on mutant or variant prostate cancer genes may be determined. In one embodiment, the
30 invention provides methods for identifying cells containing variant prostate cancer genes, e.g., determining all or part of the sequence of at least one endogenous prostate cancer genes in a cell. This may be accomplished using many sequencing techniques. In a preferred

embodiment, the invention provides methods of identifying the prostate cancer genotype of an individual, e.g., determining all or part of the sequence of at least one prostate cancer gene of the individual. This is generally done in at least one tissue of the individual, and may include the evaluation of a number of tissues or different samples of the same tissue. The method may include comparing the sequence of the sequenced prostate cancer gene to a known prostate cancer gene, e.g., a wild-type gene.

The sequence of all or part of the prostate cancer gene can then be compared to the sequence of a known prostate cancer gene to determine if differences exist. This can be done using many known homology programs, such as Bestfit, etc. In a preferred embodiment, the presence of a difference in the sequence between the prostate cancer gene of the patient and the known prostate cancer gene correlates with a disease state or a propensity for a disease state, as outlined herein.

In a preferred embodiment, the prostate cancer genes are used as probes to determine the number of copies of the prostate cancer gene in the genome.

In another preferred embodiment, the prostate cancer genes are used as probes to determine the chromosomal localization of the prostate cancer genes. Information such as chromosomal localization finds use in providing a diagnosis or prognosis in particular when chromosomal abnormalities such as translocations, and the like are identified in the prostate cancer gene locus.

Administration of pharmaceutical and vaccine compositions

In one embodiment, a therapeutically effective dose of a prostate cancer protein or modulator thereof, is administered to a patient. By "therapeutically effective dose" herein is meant a dose that produces effects for which it is administered. The exact dose will depend on the purpose of the treatment, and will be ascertainable by one skilled in the art using known techniques (e.g., Ansel, et al. (1992) Pharmaceutical Dosage Forms and Drug Delivery; Lieberman (1993) Pharmaceutical Dosage Forms (vols. 1-3, Dekker, ISBN 0824770846, 082476918X, 0824712692, 0824716981; Lloyd (1999) The Art, Science and Technology of Pharmaceutical Compounding Amer. Pharma. Assn.; and Pickar (1999) Dosage Calculations Thomson). Adjustments for prostate cancer degradation, systemic versus localized delivery, and rate of new protease synthesis, as well as the age, body weight, general health, sex, diet, time of administration, drug interaction, and the severity of the

condition may be necessary, and will be ascertainable with routine experimentation by those skilled in the art. U.S. Patent Application N. 09/687,576 further discloses the use of compositions and methods of diagnosis and treatment in prostate cancer is hereby expressly incorporated by reference.

5 A "patient" for the purposes of the present invention includes both humans and other animals, particularly mammals. Thus the methods are applicable to both human therapy and veterinary applications. In the preferred embodiment the patient is a mammal, preferably a primate, and in the most preferred embodiment the patient is human. The patient typically will suffer from a prostate proliferative disorder, e.g., malignant or non-malignant, and may
10 include cancer of other related conditions or disorders.

The administration of the prostate cancer proteins and modulators thereof of the present invention can be done in a variety of ways as discussed above, including, but not limited to, orally, subcutaneously, intravenously, intranasally, transdermally, intraperitoneally, intramuscularly, intrapulmonary, vaginally, rectally, or intraocularly. In
15 some instances, e.g., in the treatment of wounds and inflammation, the prostate cancer proteins and modulators may be directly applied as a solution or spray, or via catheter.

The pharmaceutical compositions of the present invention comprise a prostate cancer protein in a form suitable for administration to a patient. In the preferred embodiment, the pharmaceutical compositions are in a water soluble form, such as being present as
20 pharmaceutically acceptable salts, which is meant to include both acid and base addition salts. "Pharmaceutically acceptable acid addition salt" refers to those salts that retain the biological effectiveness of the free bases and that are not biologically or otherwise undesirable, formed with inorganic acids such as hydrochloric acid, hydrobromic acid, sulfuric acid, nitric acid, phosphoric acid and the like, and organic acids such as acetic acid,
25 propionic acid, glycolic acid, pyruvic acid, oxalic acid, maleic acid, malonic acid, succinic acid, fumaric acid, tartaric acid, citric acid, benzoic acid, cinnamic acid, mandelic acid, methanesulfonic acid, ethanesulfonic acid, p-toluenesulfonic acid, salicylic acid, and the like. "Pharmaceutically acceptable base addition salts" include those derived from inorganic bases such as sodium, potassium, lithium, ammonium, calcium, magnesium, iron, zinc, copper,
30 manganese, aluminum salts, and the like. Particularly preferred are the ammonium, potassium, sodium, calcium, and magnesium salts. Salts derived from pharmaceutically acceptable organic non-toxic bases include salts of primary, secondary, and tertiary amines,

substituted amines including naturally occurring substituted amines, cyclic amines and basic ion exchange resins, such as isopropylamine, trimethylamine, diethylamine, triethylamine, tripropylamine, and ethanolamine.

The pharmaceutical compositions may also include one or more of the following:

5 carrier proteins such as serum albumin; buffers; fillers such as microcrystalline cellulose, lactose, corn and other starches; binding agents; sweeteners and other flavoring agents; coloring agents; and polyethylene glycol.

The pharmaceutical compositions can be administered in a variety of unit dosage forms depending upon the method of administration. For example, unit dosage forms

10 suitable for oral administration include, but are not limited to, powder, tablets, pills, capsules and lozenges. It is recognized that prostate cancer protein modulators (e.g., antibodies, antisense constructs, ribozymes, small organic molecules, etc.) when administered orally, should be protected from digestion. This is typically accomplished either by complexing the molecule(s) with a composition to render it resistant to acidic and enzymatic hydrolysis, or by

15 packaging the molecule(s) in an appropriately resistant carrier, such as a liposome or a protection barrier. Means of protecting agents from digestion are well known in the art.

The compositions for administration will commonly comprise a prostate cancer protein modulator dissolved in a pharmaceutically acceptable carrier, preferably an aqueous carrier. A variety of aqueous carriers can be used, e.g., buffered saline and the like. These

20 solutions are typically sterile and generally free of undesirable matter. These compositions may be sterilized by conventional, well known sterilization techniques. The compositions may contain pharmaceutically acceptable auxiliary substances as required to approximate physiological conditions such as pH adjusting and buffering agents, toxicity adjusting agents and the like, e.g., sodium acetate, sodium chloride, potassium chloride, calcium chloride,

25 sodium lactate, and the like. The concentration of active agent in these formulations can vary widely, and will be selected primarily based on fluid volumes, viscosities, body weight, and the like in accordance with the particular mode of administration selected and the patient's needs (e.g., (1980) Remington's Pharmaceutical Science (15th ed.); and Hardman, et al. (eds. 2001) Goodman & Gilman: The Pharmacological Basis of Therapeutics McGraw-Hill.

30 Thus, a typical pharmaceutical composition for intravenous administration would be about 0.1 to 10 mg per patient per day. Dosages from 0.1 up to about 100 mg per patient per day may be used, particularly when the drug is administered to a secluded site and not into

the blood stream, such as into a body cavity or into a lumen of an organ. Substantially higher dosages are possible in topical administration. Actual methods for preparing parenterally administrable compositions will be known or apparent to those skilled in the art, e.g., Remington's Pharmaceutical Science and Goodman and Gilman: The Pharmacological Basis
 5 of Therapeutics, supra.

The compositions containing modulators of prostate cancer proteins can be administered for therapeutic or prophylactic treatments. In therapeutic applications, compositions are administered to a patient suffering from a disease (e.g., a cancer) in an amount sufficient to cure or at least partially retard or arrest the disease and its complications.
 10 An amount adequate to accomplish this is defined as a "therapeutically effective dose." Amounts effective for this use will depend upon the severity of the disease and the general state of the patient's health. Single or multiple administrations of the compositions may be administered depending on the dosage and frequency as required and tolerated by the patient. The composition should provide a sufficient quantity of the agents of this invention to
 15 effectively treat the patient. An amount of modulator that is capable of preventing or slowing the development of cancer in a mammal is referred to as a "prophylactically effective dose." The particular dose required for a prophylactic treatment will depend upon the medical condition and history of the mammal, the particular cancer being prevented, as well as other factors such as age, weight, gender, administration route, efficiency, etc. Such prophylactic
 20 treatments may be used, e.g., in a mammal who has previously had cancer to prevent a recurrence of the cancer, or in a mammal who is suspected of having a significant likelihood of developing cancer, e.g., based partly on gene expression profiles.

It will be appreciated that the present prostate cancer protein-modulating compounds can be administered alone or in combination with additional prostate cancer modulating
 25 compounds or with other therapeutic agent, e.g., other anti-cancer agents or treatments.

In numerous embodiments, one or more nucleic acids, e.g., polynucleotides comprising nucleic acid sequences set forth in Tables 1A-4 such as antisense polynucleotides, silencing RNA, or ribozymes, will be introduced into cells, in vitro or in vivo. The present invention provides methods, reagents, vectors, and cells useful for expression of prostate
 30 cancer-associated polypeptides and nucleic acids using in vitro (cell-free), ex vivo or in vivo (cell or organism-based) recombinant expression systems.

The particular procedure used to introduce the nucleic acids into a host cell for expression of a protein or nucleic acid is application specific. Many procedures for introducing foreign nucleotide sequences into host cells may be used. These include the use of calcium phosphate transfection, spheroplasts, electroporation, liposomes, microinjection, plasma vectors, viral vectors, and many other well known methods for introducing cloned genomic DNA, cDNA, synthetic DNA, or other foreign genetic material into a host cell (see, e.g., Berger and Kimmel (1987) Guide to Molecular Cloning Techniques from Methods in Enzymology (vol. 152) Academic Press; Ausubel, et al., (eds. supplemented through 1999) Current Protocols Lippincott; and Sambrook, et al. (1989) Molecular Cloning: A Laboratory Manual (2d ed., Vol. 1-3) CSH Press.

In a preferred embodiment, prostate cancer proteins and modulators are administered as therapeutic agents, and can be formulated as outlined above. Similarly, prostate cancer genes (including both the full-length sequence, partial sequences, or regulatory sequences of the prostate cancer coding regions) can be administered in a gene therapy application. These prostate cancer genes can include antisense applications, either as gene therapy (i.e., for incorporation into the genome) or as antisense compositions, as will be appreciated by those in the art.

Prostate cancer polypeptides and polynucleotides can also be administered as vaccine compositions to stimulate HTL, CTL, and antibody responses.. Such vaccine compositions can include, e.g., lipidated peptides (see, e.g., Vitiello, et al. (1995) J. Clin. Invest. 95:341-349), peptide compositions encapsulated in poly(DL-lactide-co-glycolide) ("PLG") microspheres (see, e.g., Eldridge, et al. (1991) Molec. Immunol. 28:287-294; Alonso, et al. (1994) Vaccine 12:299-306; Jones, et al. (1995) Vaccine 13:675-681), peptide compositions contained in immune stimulating complexes (ISCOMS) (see, e.g., Takahashi, et al. (1990) Nature 344:873-875; Hu, et al. (1998) Clin Exp Immunol. 113:235-243), multiple antigen peptide systems (MAPs) (see, e.g., Tam (1988) Proc. Natl. Acad. Sci. USA 85:5409-5413; Tam (1996) J. Immunol. Methods 196:17-32), peptides formulated as multivalent peptides; peptides for use in ballistic delivery systems, typically crystallized peptides, viral delivery vectors (Perkus, et al., p. 379, in Kaufmann (ed. 1996) Concepts in vaccine development de Gruyter; Chakrabarti, et al. (1986) Nature 320:535-537; Hu, et al. (1986) Nature 320:537-540; Kieny, et al. (1986) AIDS Bio/Technology 4:790-xxx; Top, et al. (1971) J. Infect. Dis. 124:148-154; Chanda, et al. (1990) Virology 175:535-547), particles of viral or synthetic

Vaccine compositions often include adjuvants. Many adjuvants contain a substance designed to protect the antigen from rapid catabolism, such as aluminum hydroxide or mineral oil, and a stimulator of immune responses, such as lipid A, Bordetella pertussis or Mycobacterium tuberculosis derived proteins. Certain adjuvants are commercially available as, e.g., Freund's Incomplete Adjuvant and Complete Adjuvant (Difco Laboratories, Detroit, MI); Merck Adjuvant 65 (Merck and Company, Inc., Rahway, NJ); AS-2 (SmithKline Beecham, Philadelphia, PA); aluminum salts such as aluminum hydroxide gel (alum) or aluminum phosphate; salts of calcium, iron or zinc; an insoluble suspension of acylated tyrosine; acylated sugars; cationically or anionically derivatized polysaccharides; polyphosphazenes; biodegradable microspheres; monophosphoryl lipid A, and quil A. Cytokines, such as GM-CSF, interleukin-2, -7, -12, and other like growth factors, may also be used as adjuvants.

For therapeutic or prophylactic immunization purposes, the peptides of the invention can be expressed by viral or bacterial vectors. Examples of expression vectors include

attenuated viral hosts, such as vaccinia or fowlpox. This approach involves the use of vaccinia virus, e.g., as a vector to express nucleotide sequences that encode prostate cancer polypeptides or polypeptide fragments. Upon introduction into a host, the recombinant vaccinia virus expresses the immunogenic peptide, and thereby elicits an immune response.

- 5 Vaccinia vectors and methods useful in immunization protocols are described in, e.g., U.S. Patent No. 4,722,848. Another vector is BCG (Bacille Calmette Guerin). BCG vectors are described in Stover, et al. (1991) Nature 351:456-460. A wide variety of other vectors useful for therapeutic administration or immunization, e.g., adeno and adeno-associated virus vectors, retroviral vectors, Salmonella typhi vectors, detoxified anthrax toxin vectors, and the like, will be apparent to those skilled in the art from the description herein (see, e.g., Shata, et al. (2000) Mol. Med. Today 6:66-71; Shedlock, et al. (2000) J. Leuk. Biol. 68:793-806; Hipp, et al. (2000) In Vivo 14:571-85).
- 10

Methods for the use of genes as DNA vaccines are well known, and include placing a prostate cancer gene or portion of a prostate cancer gene under the control of a regulatable promoter or a tissue-specific promoter for expression in a prostate cancer patient. The prostate cancer gene used for DNA vaccines can encode full-length prostate cancer proteins, but more preferably encodes portions of the prostate cancer proteins including peptides derived from the prostate cancer protein. In one embodiment, a patient is immunized with a DNA vaccine comprising a plurality of nucleotide sequences derived from a prostate cancer gene. For example, prostate cancer-associated genes or sequence encoding subfragments of a prostate cancer protein are introduced into expression vectors and tested for their immunogenicity in the context of Class I MHC and an ability to generate cytotoxic T cell responses. This procedure may provide for production of cytotoxic T lymphocyte responses against cells which present antigen, including intracellular epitopes.

- 25 In a preferred embodiment, the DNA vaccines include a gene encoding an adjuvant molecule with the DNA vaccine. Such adjuvant molecules include cytokines that increase the immunogenic response to the prostate cancer polypeptide encoded by the DNA vaccine. Additional or alternative adjuvants are available.
- 30

In another preferred embodiment prostate cancer genes find use in generating animal models of prostate cancer. When the prostate cancer gene identified is repressed or diminished in cancer tissue, gene therapy technology, e.g., wherein antisense RNA directed to the prostate cancer gene will also diminish or repress expression of the gene. Animal

models of prostate cancer find use in screening for modulators of a prostate cancer-associated sequence or modulators of prostate cancer. Similarly, transgenic animal technology including gene knockout technology, e.g., as a result of homologous recombination with an appropriate gene targeting vector, will result in the absence or increased expression of the prostate cancer protein. When desired, tissue-specific expression or knockout of the prostate cancer protein may be necessary.

It is also possible that the prostate cancer protein is overexpressed in prostate cancer. As such, transgenic animals can be generated that overexpress the prostate cancer protein. Depending on the desired expression level, promoters of various strengths can be employed to express the transgene. Also, the number of copies of the integrated transgene can be determined and compared for a determination of the expression level of the transgene. Animals generated by such methods find use as animal models of prostate cancer and are additionally useful in screening for modulators to treat prostate cancer.

Kits for Use in Diagnostic and/or Prognostic Applications

For use in diagnostic, research, and therapeutic applications suggested above, kits are also provided by the invention. In the diagnostic and research applications such kits may include one of the following: assay reagents, buffers, prostate cancer-specific nucleic acids or antibodies, hybridization probes and/or primers, antisense polynucleotides, silencing RNA, ribozymes, dominant negative prostate cancer polypeptides or polynucleotides, small molecules inhibitors of prostate cancer-associated sequences, etc. A therapeutic product may include sterile saline or another pharmaceutically acceptable emulsion and suspension base.

In addition, the kits may include instructional materials containing instructions (i.e., protocols) for the practice of the methods of this invention. While the instructional materials typically comprise written or printed materials they are not limited to such. A medium capable of storing such instructions and communicating them to an end user is contemplated by this invention. Such media include, but are not limited to electronic storage media (e.g., magnetic discs, tapes, cartridges, chips), optical media (e.g., CD ROM), and the like. Such media may include addresses to internet sites that provide such instructional materials.

The present invention also provides for kits for screening for modulators of prostate cancer-associated sequences. Such kits can be prepared from readily available materials and reagents. For example, such kits can comprise one or more of the following materials: a

prostate cancer-associated polypeptide or polynucleotide, reaction tubes, and instructions for testing prostate cancer-associated activity. Optionally, the kit contains biologically active prostate cancer protein. A wide variety of kits and components can be prepared according to the present invention, depending upon the intended user of the kit and the particular needs of
5 the user. Diagnosis would typically involve evaluation of a plurality of genes or products. The genes will be selected based on correlations with important parameters in disease which may be identified in historical or outcome data.

EXAMPLES

Example 1: Gene Chip Analyses of Expression Profiles

Molecular profiles of various normal and cancerous tissues were determined and analyzed using gene chips. RNA was isolated and gene chip analysis was performed as described (Glynn, et al. (2000) *Nature* 403:672-676; Zhao, et al. (2000) *Genes Dev.* 14:981-993).

EXAMPLE 2: Identification of androgen dependent/independent genes

To identify gene expression changes during the transition from androgen-dependent to androgen-independent prostate cancer, oligonucleotide microarrays ("K" chips or Affymetrix Eos Hu03) were interrogated with cRNAs derived from the human CWR22 prostate cancer xenograft model propagated in nude mice (Pretlow, et al. (1993) *J. Natl. Cancer Inst.* 85:394-398). The CWR22 xenograft is androgen-dependent when grown in male Nude mice. Androgen-independent sub-lines can be derived by first establishing androgen-dependent tumors in male mice. The mice are then castrated to remove the primary source of growth stimulus (androgen), resulting in tumor regression. Within 3-10 months molecular events prompt the tumors to relapse and start growing as androgen-independent tumors. See, e.g., Nagabhushan, et al. (1996) *Cancer Res.* 56:3042-3046; Amler, et al. (2000) *Cancer Res.* 60:6134-6141; and Bubendorf, et al. (1999) *J. Natl. Cancer Inst.* 91:1758-1764.

Using the CWR22 xenograft model, tumors were grown subcutaneously in male nude mice. Tumors were harvested at different times after castration. The time points post-castration included (in days): 0, 1, 3, 4, 5, 10, 30, 40, 50, 51, 52, 59, 60, 61, 70, 79, 80, 82, 120, and 125. Analyses also included established androgen-independent xenografts. Castration resulted in tumor regression. At day 120 and thereafter, the tumors relapsed and started growing in the absence of androgen.

cRNAs were generated by in vitro transcription assays (IVTs) from the different samples and were hybridized to the oligonucleotide microarrays (Affymetrix Eos Hu03). Hybridization was measured by the average fluorescence intensity (AI), which is directly proportional to the expression level of the gene.

Two types of analyses were applied to the results:

Analysis A:

The samples were divided into different time groups which included the following time points post castration (in days): 1-5, 10, 30-40, 50-82, 120-125. To identify changes in gene expression, the following calculations were made:

1. The median (or mean, in case there were only 2 samples in a group) was calculated for each group.
2. The medians (or means) for each group was compared to one-another.
3. Genes were selected that exhibited a minimum 2 fold difference in the median (or mean) between any of the groups.
4. The change in gene expression over time was analyzed for each selected gene to look for specific pattern changes.

Only genes with an interesting expression pattern during the androgen-ablation time course were selected as potential new therapeutic targets and/or diagnostic markers. Among the 70,000 gene clusters present on Hu01 and Hu02, we identified 820 gene clusters with the desired expression patterns. These expression patterns can be broadly defined into the following categories:

1. Genes that are expressed early in the time course, then drop off in expression, and then express again with emergence of androgen-independence (hi-lo-hi pattern in Table 1A).
2. Genes that are expressed early in the time course, then drop off in expression, and do not express again with emergence of androgen-independence (hi-lo-lo pattern in Table 1A).
3. Genes that are not expressed early in the time course, but express only with emergence of androgen-independence (lo-lo-hi pattern in Table 1A).
4. Genes that are not expressed early in the time course, but then express as androgen is withdrawn and continue to express with emergence of androgen-independence (lo-hi-hi pattern in Table 1A).
5. Genes that are not expressed early in the time course, but then express as androgen is withdrawn and drop off again with emergence of androgen-independence (lo-hi-lo pattern in Table 1A).

Group 1 is characterized by cell-cycle regulating genes, such as those encoding cyclin B1, p21/WAF1, CDC18-homolog, cyclin A2, cyclin D1, and possible growth factors such as hAG2 (anterior gradient 2 homolog) among others. This indicates that interruption of growth factor and/or cell cycle pathways prevents the emergence of androgen-independent disease, making group 1 genes good targets for treating advanced prostate cancer.

Group 2 represents genes that are androgen-dependent, and do not re-express due to the lack of androgen signal in the androgen-independent phenotype. This group includes genes encoding proteins such as Fibronectin 1, which has been previously shown to be down-regulated with androgen-withdrawal (Amler, et al. (2000) Cancer Res. 60:6134-6141).

Group 3 represents genes that are up-regulated by signals that induce the androgen-independent phenotype. This group includes genes encoding stanniocalcin 2, c-fos proto-oncogene product, vascular endothelial growth factor, the cell surface protein transmembrane 4 superfamily member 1 and adrenomedullin among others. Adrenomedullin has recently been shown to act as an autocrine growth factor for the androgen-independent prostate cancer cell line DU145 (Rocchi, et al. (2001) Cancer Res. 61:1196-1206), indicating that its up-regulation is critical for supporting an androgen-independent phenotype. Blocking adrenomedullin function, and/or other genes in this group, prevents the growth of androgen-independent tumor cells.

Group 4 represents genes that are androgen-repressed and are only expressed in the absence of androgen. This group includes genes encoding the protein tyrosine phosphatase interacting protein liprin-alpha 2, the CD24 antigen, and the catalytic subunit for phosphatidylinositol 4-kinase amongst others. Patients that are treated for advanced prostate cancer by hormone-ablation may have in their bodies cells that have survived hormone-ablation and are likely to up-regulate genes that belong to Group 4. Therefore, Group 4 gene products are particularly good therapeutic targets for treating patients undergoing hormone-ablation therapy.

Group 5 represents genes that are involved in regulating signals that induce an androgen-independent phenotype. This group includes genes encoding Rab2 (a Ras-like G protein), the Son of Sevenless homolog (a GTP/GDP exchange factor involved in activating Ras-like proteins), and the p85 regulatory subunit for phosphoinositide-3-kinase (PI3-kinase). The PI3-kinase pathway has been implicated in providing a survival signal to the prostate cancer cell line LNCaP (Lin, et al. (1999) Cancer Res. 59:2891-2897). This indicates that ras-like signals and signals dependent on PI3-kinase are involved in inducing the androgen-independent phenotype. For that reason, Group 5 gene products are particularly good therapeutic targets for treating patients undergoing hormone-ablation therapy.

Analysis B:

For the second analysis, the samples were divided into 4 time groups which included the following time points post castration (in days): 0-1, 3-5, 10-82, >120. To identify changes in gene expression, the following analysis was performed:

1. Genes were selected that exhibited a minimum of 100 AI units at the 90th percentile
5 expression level of samples.
2. The group mean expression levels for each gene were calculated. The genes were further sub-selected to exhibit a minimum 3 fold difference between the group means.
3. An analysis of variance was then performed on selected genes. From the original 59,680 gene clusters present on the Hu03 gene chip, only about 1165 genes with a P value of < 0.01
10 were identified that also exhibited the above mentioned parameters.
4. A method was then employed for calculating the positive false discovery rate (pFDR), i.e., an estimate of the proportion of false-positives present in a set of findings (Storey and Tibshirani (2001) Technical Report, Department of Statistics, Stanford University, CA). This technique was developed explicitly for use with microarray data. The procedure
15 involves randomly assigning the membership status of each sample to a group and re-performing the analysis of variance. In each simulation, the number of group members (6 for Group 1, 9 for group 2, 15 for group 3, and 4 for group 4) remained constant, but these designations were shuffled and assigned to each sample at random. The permutation was performed 1000 times, and for each simulation, the number of findings at $P < 0.01$ was noted.
20 The number of false positives under null conditions, was then divided by the number of actual findings ($n=1165$ genes) to obtain an estimate of the proportion of false positive findings. After the application of a correction factor, the final estimate for the pFDR was about 1%. Thus, one can expect that approximately 12 of the 1165 findings are false positives.
- 25 5. The approximately 1165 genes were clustered by expression pattern to identify specific pattern changes. Only genes with an interesting expression pattern during the androgen-ablation time course were selected as potential new therapeutic targets and/or diagnostic markers. These expression patterns can be broadly defined into the following categories:
 1. Genes that are expressed early in the time course of androgen withdrawal, then drop off in
30 expression, and then express again with emergence of androgen-independence (hi-lo-lo-hi pattern in Table 2A).

2. Genes that are expressed early in the time course, then drop off in expression immediately after androgen-withdrawal, and do not express again with emergence of androgen-independence (hi-lo-lo-lo pattern in Table 2A).
3. Genes that are expressed early in the time course, then drop off in expression after several
- 5 days of androgen withdrawal, and do not express again with emergence of androgen-independence (hi-hi-lo-lo pattern in Table 2A).
4. Genes that are not expressed early in the time course, but express only with emergence of androgen-independence (lo-lo-lo-hi pattern in Table 2A).
5. Genes that are not expressed early in the time course, but then express as androgen is
- 10 withdrawn and continue to express with emergence of androgen-independence (lo-lo-hi-hi pattern in Table 2A).
6. Genes that are not expressed early in the time course, but then express as androgen is withdrawn and drop off again with emergence of androgen-independence (lo-lo-hi-lo pattern in Table 2A).

15 Group 1 is characterized by cell-cycle regulating genes and cell growth promoting genes, such as those encoding cyclin B1 and CDC45 among others, growth factors/hormones such as hAG2 (anterior gradient 2 homolog), adrenomedullin, and stanniocalcin 2 among others, and growth factor receptors, such as the bone morphogenic protein receptor type 1B (BMP-R1B) and the endothelial differentiation lysophosphatidic acid G-protein-coupled

20 receptor 7 among others. Adrenomedullin has recently been shown to act as an autocrine growth factor for the androgen-independent prostate cancer cell line DU145 (Rocchi, et al. (2001) Cancer Res. 61:1196-1206), indicating that its up-regulation is critical for supporting an androgen-independent phenotype. This indicates that interruption of growth factor and/or cell cycle pathways prevents the emergence of androgen-independent disease, making group

25 1 genes good targets for treating both localized and advanced prostate cancer and related conditions.

 Group 2 represents genes that are androgen-dependent, and do not re-express due to the lack of androgen signal in the androgen-independent phenotype. This group includes

30 genes encoding proteins such as the endothelial protein C receptor (EPCR) and the potassium intermediate/small conductance calcium-activated channel (subfamily N, member 2). These genes represent targets for treating androgen-dependent prostate cancer and related conditions.

Group 3 also represents genes that are androgen-dependent, and do not re-express due to the lack of androgen signal in the androgen-independent phenotype. This group includes genes encoding proteins such as Fibronectin 1, which has been previously shown to be down-regulated with androgen-withdrawal (Amler, et al. (2000) Cancer Res. 60:6134-6141), and
5 genes encoding signaling proteins such as Rho GTPase activating protein 1. These genes represent targets for treating androgen-dependent prostate cancer and related conditions.

Group 4 represents genes that are up-regulated by signals that induce and maintain the androgen-independent phenotype. This group includes genes encoding potential growth promoting proteins such as chemokine-like factor (Unigene ID Hs.15159), colon cancer-associated protein Mic1, and the mitogen-activated protein kinase-activated protein kinase 2.
10 Blocking function of these proteins, and/or other genes in this group, prevents the growth of androgen-independent tumor cells and related conditions.

Group 5 represents genes that are androgen-repressed and are only expressed in the absence of androgen or that are induced by the absence of androgen. This group includes
15 genes encoding transcriptional regulators such as the androgen receptor, the DNA activated protein kinase (catalytic subunit), and nuclear factor related to kappa B binding protein (NFKB), among others. Patients that are treated for advanced prostate cancer by hormone-ablation may have in their bodies cells that have survived hormone-ablation and are likely to up-regulate genes that belong to Group 5. Therefore, Group 5 gene products are particularly
20 good therapeutic targets for treating patients undergoing hormone-ablation therapy.

Group 6 represents genes that are involved in regulating signals that are induced during androgen withdrawal and that induce an androgen-independent phenotype. This group includes genes encoding signaling molecules such as phosphoinositide-3-kinase (class 2, alpha polypeptide), signal transducer and activator of transcription 2 (STAT2), phospholipase
25 A2 (group IIA) and the protein tyrosine phosphatase interacting protein liprin-alpha 2, cell surface receptors such as gamma-aminobutyric acid (GABA) A receptor epsilon subunit, G protein-coupled receptor 48, and immune function proteins such as the major histocompatibility complex class II DR alpha. The PI3-kinase pathway has been implicated in providing a survival signal to the prostate cancer cell line LNCaP (Lin, et al. (1999) Cancer
30 Res. 59:2891-2897). This indicates that ras-like signals and signals dependent on PI3-kinase are involved in inducing the androgen-independent phenotype. For that reason, Group 6 gene

WO 02/098358

PCT/US02/17594

products are particularly good therapeutic targets for treating patients undergoing hormone-ablation therapy.

person).

prediction. Nucleotide locations of each predicted exon are also listed.

Pkey	ExAcn	UnigeneID	Unigene Title	palcm
------	-------	-----------	---------------	-------

Ni-30-Ni

315618	AJ287341	*Hs.154029
11590	AA378597	*Hs.1539
132959	AW014195	*Hs.61472
103195	AA351647	*Hs.2642
100368	D79987	*Hs.153479
103177	BE244377	*Hs.48676
109141	AF174620	*Hs.193390
100676	X02761	*Hs.287820
100254	AA452181	*Hs.77643
133688	U71321	*Hs.7557
107129	AC004770	*Hs.47656
102696	BE540274	*Hs.235
101753	L11144	*Hs.1907
101897	AA317089	*Hs.597
133512	L18861	*Hs.147097
133980	X14852	*Hs.147097
101600	BE561617	*Hs.119192
101332	J04088	*Hs.156346
132967	AA316181	*Hs.61635
122726	L15474	*Hs.132068
106925	AK002011	*Hs.57558
105643	BE621719	*Hs.173902
116028	I59799	*Hs.42844
105437	AF151078	*Hs.25199
122612	AF053306	*Hs.68656
131991	AF053306	*Hs.36708
136015	AW361638	*Hs.278338
102208	U22961	*Hs.10744
100744	AL119584	*Hs.75816
100447	NM_014767	*Hs.74583
116878	D21282	*Hs.75337
130350	AA369501	*Hs.239138
101045	J05614	*Hs.101169
101544	X31169	*Hs.101169
113674	NM_014214	*Hs.5753
102260	NL039104	*Hs.159567
100154	H00720	*Hs.21892
100189	BE592298	*Hs.17627
100372	NM_014791	*Hs.184339
100387	D63777	*Hs.75137
131514	BE270734	*Hs.2795
102639	VZ7518	*Hs.234488
105811	BE517895	*Hs.266152
101013	BE300094	*Hs.227751
124148	BE300094	*Hs.227751
102988	AL078611	*Hs.154672
130149	AW067806	*Hs.172655
114767	AB858865	*Hs.154443
129168	AI132988	*Hs.105052
106011	BE091526	*Hs.16244
103023	AW050470	*Hs.117950
102806	BE242818	*Hs.178605
318617	AW247252	*Hs.75514
101588	M81740	*Hs.75212
102076	BE256797	*Hs.176665
102022	BE294407	*Hs.176665
101032	BE206854	*Hs.46039
130553	AF062649	*Hs.252587
101626	V57399	*Hs.44
101992	X30725	*Hs.77597
132184	AI752248	*Hs.41770
101306	BE267931	*Hs.78996
110018	AA631143	*Hs.178609
101840	AA236291	*Hs.183583
332640	BE568452	*Hs.5101
132543	BE568452	*Hs.5101
101118	AA371931	*Hs.77422
109166	AA219691	*Hs.73625
100630	AC004770	*Hs.4766
107050	BE514410	*Hs.23044
321693	AA227069	*Hs.173737
101148	NM_002923	*Hs.78944
130957	AA383092	*Hs.1808
102676	NM_001034	*Hs.75319
103131	BE539069	*Hs.2362
102212	AW411491	*Hs.75069
104254	AW411425	*Hs.180655
102745	BE518138	*Hs.24447
102012	BE259035	*Hs.118400
102522	BE250944	*Hs.183556
132994	AA112748	*Hs.279055
101971	Z49105	*Hs.289105

hHcH factor Hes4	h2-h2
HSPC150 protein similar to ubiquitin-con	h2-h2
ESTs, Weakly similar to unknown [S.cerev	h2-h2
eukaryotic translation elongation factor	h2-h2
extra spindle poles, S. cerevisiae, homo	h2-h2
laminase-1-phosphatase laminase transferase	h2-h2
F-box protein [Es20]	h2-h2
fibronectin 1	h2-h2
FK506-binding protein 1B (12.6 kD)	h2-h2
FK506-binding protein 5	h2-h2
flag structure-specific endonuclease 1	h2-h2
forkhead box M1	h2-h2
galanin	h2-h2
glutamic-oxaloacetic transaminase 1, sol	h2-h2
gu-Hamann Gulf-mip gene, clone 1.	h2-h2
H2A histone family, member X	h2-h2
H2A histone family, member Z	h2-h2
topoisomerase (DNA) II alpha (170kD)	h2-h2
alpha transmembrane epithelial antigen of	h2-h2
fatty acid desaturase 1	h2-h2
hypothetical protein FLJ11149	h2-h2
KIAA0603 gene product	h2-h2
thiorodovir-like	h2-h2
hypothetical protein	h2-h2
binding uninhibited by benzimidazoles 1	h2-h2
binding uninhibited by benzimidazoles 1	h2-h2
LGN protein	h2-h2
gli-Human mRNA clone with similarity to L	h2-h2
saladin 1	h2-h2
KIAA0275 gene product	h2-h2
nucleolar phosphoprotein p130	h2-h2
pre-B-cell colony-enhancing factor	h2-h2
gli-Human proliferating cell nuclear anti	h2-h2
gli-Human prolamin-Glu carboxylase beta-	h2-h2
inositol(myo)-1-(or 4)-monophosphatase 2	h2-h2
karyopherin alpha (2) (RAG cohort 1, impor	h2-h2
KIAA0101 gene product	h2-h2
KIAA0112 protein; homolog of yeast ribos	h2-h2
KIAA0175 gene product	h2-h2
KIAA0193 gene product	h2-h2
isolate dehydrogenase A	h2-h2
isolate dehydrogenase B	h2-h2
protein phosphatase 1, regulatory (inhib	h2-h2
lectin, galactoside-binding, soluble, 1	h2-h2
lectin, galactoside-binding, soluble, 1	h2-h2
methylene tetrahydrofolate dehydrogenase	h2-h2
methylene tetrahydrofolate dehydrogenase	h2-h2
minichromosome maintenance deficient (S,	h2-h2
chromosome 14 open reading frame 2	h2-h2
mitotic spindle coiled-coil related prot	h2-h2
multifunctional polysphatase similar to S	h2-h2
nuclear RNA helicase, DCC2 variant of DE	h2-h2
nucleotide phosphorylase	h2-h2
ornithine decarboxylase 1	h2-h2
cyclin-dependent kinase inhibitor 1A (p2	h2-h2
phosphatidylcholine, platelet	h2-h2
phosphoglycerate mutase 2 (muscle)	h2-h2
plutaryl tumor-transforming 1	h2-h2
pleiotrophin (heparin binding growth fac	h2-h2
polo (Drosophila)-like kinase	h2-h2
procollagen-lysine, 2-oxoglutarate 5-di	h2-h2
proliferating cell nuclear antigen	h2-h2
ESTs	h2-h2
protein regulator of cytokinesis 1	h2-h2
protein regulator of cytokinesis 1	h2-h2
proteolipid protein 2 (colonic epitheliu	h2-h2
RAB5 interceding, kinesin-like (rakikines	h2-h2
flag structure-specific endonuclease 1	h2-h2
RNASE1 (S. cerevisiae) homolog (E.coli Ra	h2-h2
ras-related G3b tubulin mon subunit	h2-h2
regulator of G-protein signalling 2, 24k	h2-h2
replication protein A3 (14kD)	h2-h2
ribonucleoside reductase M2 polypeptide	h2-h2
S100 calcium-binding protein P	h2-h2
serine hydroxymethyltransferase 2 (mink	h2-h2
serine/threonine kinase 12	h2-h2
sigma receptor (SR31747 binding prot	h2-h2
slinged (Drosophila)-like (see archon fac	h2-h2
solute carrier family 1 (neutral amino a	h2-h2
clone HQ0310 PRO0310p1	h2-h2
synovial stroma, X chromosome 2	h2-h2

WO 02/098358

PCT/US02/17594

	128646	AA318181	Ha. 91635	six transmembrane epithelial antigen of	hi-to-hi
	103058	XJ7348	Ha. 184510	stratelin	hi-to-hi
	102632	U86519	Ha. 260591	SWI/SNF related, matrix associated, acti	hi-to-hi
5	103299	AF230662	Ha. 289105	synovial sarcoma, X breakpoint 2	hi-to-hi
	128920	AA622037	Ha. 166468	programmed cell death 5	hi-to-hi
	100114	X02308	Ha. 82962	thymidylate synthetase	hi-to-hi
	102945	BE264974	Ha. 6556	tyrosid homotile receptor interacto 13	hi-to-hi
	131877	J04086	Ha. 156346	topoisomerase (DNA) II alpha (170K)	hi-to-hi
10	100856	U14134	Ha. 75113	general transcription factor IIIA	hi-to-hi
	133893	AA434699	Ha. 77355	transferrin receptor (p90, CD71)	hi-to-hi
	130135	AA311426	Ha. 21635	tubulin, gamma 1	hi-to-hi
	130291	AA478006	Ha. 154036	tumor suppressing subtransferrable candid	hi-to-hi
	128180	L32977	Ha. 3712	ubiquitin-cytochrome c reductase, Reske	hi-to-hi
15	101536	NM_006002	Ha. 77917	ubiquitin carboxyl-terminal esterase L3	hi-to-hi
	102687	NM_007019	Ha. 33002	ubiquitin carrier protein E2-C	hi-to-hi
	103658	Z19002	Ha. 37096	zinc finger protein 145 (Nuppa-like, e	hi-to-hi
				900022	hi-to-hi
	138015	AI/002744	Ha. 246315	UDP-N-acetyl-alpha-D-galactosamine: poly	hi-to-hi
20	128642	NM_001360	Ha. 11806	7-dehydrocholesterol reductase	hi-to-hi
	134369	AF207664	Ha. 8230	a disintegrin-like and metalloprotease (hi-to-hi
	300028				hi-to-hi
	125183	AV690804	Ha. 301417	AHNRAK nucleoprotein (transmyokinin)	hi-to-hi
	101768	M80899	Ha. 301417	AHNRAK nucleoprotein (transmyokinin)	hi-to-hi
25	133516	BE265133	Ha. 217493	annexin A2	hi-to-hi
	102145	AW162667	Ha. 78529	ATPase, Na+/K+ transporting, beta 1 poly	hi-to-hi
	131838	A756579	Ha. 740394	Homo sapiens clone 24651 cDNA sequence	hi-to-hi
	103554	A1878626	Ha. 323469	caveolin 1, caveolin protein, 23KDa	hi-to-hi
	323605			CHX_1c_g6608838	hi-to-hi
30	334282			CH22_FGENES.359_12	hi-to-hi
	334691			CH22_FGENES.482_5	hi-to-hi
	335140			CH22_FGENES.459_5	hi-to-hi
	336632			CH22_FGENES.555_2	hi-to-hi
	336765			CH22_FGENES.504_5	hi-to-hi
35	330851			collagen, type I, alpha 1	hi-to-hi
	134421	AU077198	Ha. 82585	collagen, type V, alpha 2	hi-to-hi
	131101	BE387681	Ha. 22381	DKFZP595M1523 protein	hi-to-hi
	124153	AU077333	Ha. 160483	erythrocyte membrane protein band 7.2 (s	hi-to-hi
	103328	AU077333	Ha. 160483	erythrocyte membrane protein band 7.2 (s	hi-to-hi
40	322336	AL137517	Ha. 305201	hypothetical protein DKFZP564O1278	hi-to-hi
	301872	H84730	Ha. 326391	ESTs, Highly similar to KIAA1437 protein	hi-to-hi
	303620	AB037858	Ha. 173484	hypothetical protein FLJ10337	hi-to-hi
	304049	T58155		glycylserine 181 Stratagene tag (937210) H	hi-to-hi
	304735	AA575453		gly-m/SH1.5.1 NCL_CGAP, Cdc Homo sapiens	hi-to-hi
45	306999	AI138628	Ha. 308058	EST, Weakly similar to zinc finger prot	hi-to-hi
	128769	AW368676	Ha. 139851	caveolin 2	hi-to-hi
	132057	AB037858	Ha. 173484	hypothetical protein FLJ10337	hi-to-hi
	114795	AB037858	Ha. 173484	hypothetical protein FLJ10337	hi-to-hi
	104204	AJ001691	Ha. 57655	hypothetical protein FLJ10329	hi-to-hi
50	105200	AA328102	Ha. 24641	cytoskeleton associated protein 2	hi-to-hi
	105493	AL047588	Ha. 10283	RNA binding motif protein 8B	hi-to-hi
	107677	AI188161	Ha. 144627	ESTs	hi-to-hi
	168890	AA768605	Ha. 47039	hypothetical protein FLJ21212	hi-to-hi
	111157	AL108720	Ha. 18946	ESTs, Highly similar to A31028 probable	hi-to-hi
55	116202	BE158395	Ha. 87069	ESTs	hi-to-hi
	120698	AW134519	Ha. 88125	ESTs	hi-to-hi
	121847	AA486258	Ha. 2789	cartilage linking protein 1	hi-to-hi
	124182	AB83471	Ha. 107801	ESTs	hi-to-hi
	128515	BE385085	Ha. 10085	type I transmembrane protein Fn14	hi-to-hi
60	130465	W19744	Ha. 180059	Homo sapiens cDNA FLJ20653 (s, clone KA	hi-to-hi
	131078	AA749230	Ha. 22666	ESTs	hi-to-hi
	131094	NM_017413	Ha. 302384	apelin, peptide ligand for APJ receptor	hi-to-hi
	134109	AA548031	Ha. 7913	ESTs	hi-to-hi
	300258	AA78933	Ha. 186260	ESTs	hi-to-hi
65	302767	H94900	Ha. 17882	ESTs	hi-to-hi
	312391	R43707	Ha. 133159	ESTs, Weakly similar to PHUSD salivary	hi-to-hi
	312689	AW460461	Ha. 203865	ESTs	hi-to-hi
	315715	AI284219	Ha. 130749	ESTs	hi-to-hi
	315843	AA679430	Ha. 191897	ESTs	hi-to-hi
70	322447	AI736759	Ha. 52620	integrin, beta 8	hi-to-hi
	322626	AB078663	Ha. 201773	ESTs	hi-to-hi
	324867	AB24707	Ha. 5521	Homo sapiens cDNA: FLJ21592 (s, clone C	hi-to-hi
	331336	AA287450	Ha. 93842	Homo sapiens cDNA: FLJ22554 (s, clone	hi-to-hi
	331353	AA853006	Ha. 88143	ESTs	hi-to-hi
75	133063	AB64133	Ha. 302212	tyrosid receptor interacting protein 15	hi-to-hi
	310304	BE267130	Ha. 311385	ESTs, Moderately similar to Y161_HUMAN IYPTOT	hi-to-hi
	108647	BE546347	Ha. 44276	homeo box C10	hi-to-hi
	124555	AA376768	Ha. 324841	hypothetical protein FLJ22622	hi-to-hi
	113623	AW953494	Ha. 3849	hypothetical protein FLJ22841 similar to	hi-to-hi
	310557	AA431786	Ha. 164192	ESTs, Weakly similar to Y161_HUMAN IYPTOT	hi-to-hi
80	302943	AS81344	Ha. 127812	ESTs, Weakly similar to T17300 hypophos	hi-to-hi
	128453	X02761	Ha. 287820	fibrinogen 1	hi-to-hi
	305222	AA670052	Ha. 169478	glyoxaldehyde-3-phosphate dehydrogenase	hi-to-hi

	134005	Z4955	Ha.7837	G-protein-coupled receptor produced protein	hi-hi
	124847	W07701	Hi.304177	Human sapirins clone FLB8503 INC02285 mRNA	hi-hi
	129387	A348027	Hi.108557	Human sapirins clone PP1057 mRNA	hi-hi
5	131762	AA74492	Hi.107787	hypothetical protein P01489	hi-hi
	129145	AA74922	Hi.107757	hypothetical protein P01489	hi-hi
	105713	A112283	Hi.184319	ESTs, Weakly similar to KIAA1000 protein	hi-hi
	118475	N58645		gizmo4f11.1 Sources fetal liver spleen	hi-hi
	118381	N64613	Hi.48894	ESTs, Weakly similar to AF151801 1 CGL-4	hi-hi
10	105057	AA134233		gizmo2f11.1 Stratagene clone (37204)	hi-hi
	129528	AB28298	Hi.27769	ESTs, VAG2769 similar to MCAF, Human MITOC	hi-hi
	124970	DE272962	Hi.106334	hypothetical protein FLJ22625	hi-hi
	130094	NM_001471	Hi.167070	gamma-aminobutylic acid (GABA) B receptor	hi-hi
	302337	X03178	Hi.182446	group-specific component (vitamin D binding	hi-hi
15	115249	AA278582	Hi.180377	Human sapirins clone P01489 and Z0385 mRNA	hi-hi
	111923	DE3833294	Hi.25925	Human sapirins clone Z3850 mRNA sequence	hi-hi
	128530	AB32995	Hi.183475	Human sapirins clone Z50501 mRNA sequence	hi-hi
	128897	A1339046	Hi.107637	hypothetical protein FLJ12806	hi-hi
	315358	AB037745	Hi.104695	KIAA1324 protein	hi-hi
	1093579	AB093579	Hi.7374	Human sapirins mRNA: cDNA DKFZ565A072 (7	hi-hi
	115094	AB333699	Hi.425442	Human sapirins mRNA: FLJ10618	hi-hi
	132883	AA573314	Hi.5897	Human sapirins mRNA: cDNA DKFZ569P1822 (7	hi-hi
	108623	AW207388	Hi.259501	KIAA081 protein	hi-hi
	130142	M56241	Hi.1612	Human sapirins mRNA: protein factor binding	hi-hi
	101859	AF188747	Hi.181350	kallikrein 2, prostatic	hi-hi
20	130426	AA55210	Hi.171195	kallikrein 3, kallikrein-specific antigen	hi-hi
	128180	AW949098	Hi.171955	kallikrein 3, (prostatic) specific antigen	hi-hi
	13482	AI.137481	Hi.125511	Human sapirins mRNA: cDNA DKFZP434F1530 (7	hi-hi
	104474	A22412	Hi.204098	Human sapirins mRNA: cDNA DKFZP434F1530 (7	hi-hi
	117921	AA021458	Hi.306480	Human sapirins mRNA: cDNA DKFZP761E1212 (1	hi-hi
30	101701	NM_002436	Hi.1861	membrane protein, palmitoylated 1 (ESD2)	hi-hi
	130368	AF127577	Hi.155017	receptor tyrosine kinase, class 1	hi-hi
	101471	AD001014	Hi.170414	protein tyrosine kinase class 1, catalytic	hi-hi
	130342	U81802	Hi.154646	phosphotyrosine 14-interacting, catalytic	hi-hi
	130760	AW379130	Hi.18593	phosphotransferase 3A	hi-hi
	101481	N85859	Hi.78422	phosphotransferase A2, group IIA (platelets,	hi-hi
35	134031	NM_005025	Hi.75858	sarins (or cytolins) protein tyrosine kinase	hi-hi
	103672	AF347891	Hi.30581	protein tyrosine phosphatase, receptor I	hi-hi
	110632	AA021458	Hi.306480	Human sapirins mRNA: cDNA DKFZP761E1212 (1	hi-hi
	136192	U83993	Hi.321708	perlecanin receptor P2X, ligand-gated ion	hi-hi
	133988	UF7276	Hi.77268	channel G	hi-hi
	134742	BE344053	Hi.78392	muscle-specific 2 (p130)	hi-hi
	100677	X08021	Hi.302177	Hsapiens mRNA for ribosomal protein L18	hi-hi
	133534	AA077115	Hi.201675	R18A binding motif protein 5	hi-hi
	133011	NM_006379	Hi.175923	sema domain, immunoglobulin domain (cys),	hi-hi
	132160	W25406	Hi.238252	sema domain, immunoglobulin homology 1	hi-hi
	103110	X06252	Hi.104144	synlysin-1 (beta-galactosidase 2	hi-hi
	130173	U38847	Hi.151518	TAR (HIV) RNA-binding protein 1	hi-hi
	127436	X06906	Hi.265816	human protein KIAA113615 fits, clone PL	hi-hi
	110520	N54068	Hi.4062	cell, galactose-binding, soluble, 5	hi-hi
	114660	AA071383	Hi.1852	zeta-zinc finger, alpha-strain fibroblast (33	hi-hi
	330541	NM_002038	Hi.285257	interferon, alpha-Inducible protein (alpha	hi-hi
	101488	AA503324	Hi.1852	alpha-phosphatase, prostatic	hi-hi
	332368	NM_004081	Hi.102	aminomethyltransferase (glycine cleavage	hi-hi
	100149	AA55210	Hi.171195	aminomethyltransferase (glycine cleavage	hi-hi
	134738	AW078091	Hi.88438	cathepsin T, L1, cathepsin (HIV-inactivin	hi-hi
	103119	X03629	Hi.2877	cathepsin 3, type 1, P-cathepsin (placenta	hi-hi
	302892	AW177698	Hi.82748	calcium-binding protein catenin-3	hi-hi
	105402	AB014680	Hi.42366	cardiolipin (cardiolipin) cholesterol sul	hi-hi
	100781	AA077114	Hi.201675	cardiolipin (cardiolipin) cholesterol sul	hi-hi
	101793	W071076	Hi.119603	CD59 antigen p18-20 antigen identified	hi-hi
	128980	AB585972	Hi.282804	Human sapirins cDNA: FL22074 fits, clone H	hi-hi
	328164			CH.04, pg.03695008	hi-hi
	320546			CH.07, pg.03690	hi-hi
	330032			CH.16, pg.036982596	hi-hi
65	330033			CH.16, pg.036982596	hi-hi
	330618			CH.02, pg.03652458	hi-hi
	337603			CH.02, CGH12, GENSCAN 16.2	hi-hi
	338661			CH.02, EMAC005000, GENSCAN 421-5	hi-hi
70	333743			CH.02, EMAC005000, GENSCAN 421-6	hi-hi
	333743			CH.02, GENES.254.3	hi-hi
	333846			CH.02, GENES.250.3	hi-hi
	333849			CH.02, GENES.250.8	hi-hi
	334221			CH.02, GENES.390.1	hi-hi
	334222			CH.02, GENES.360.3	hi-hi
75	334578			CH.02, GENES.406.1	hi-hi
	336922			CH.02, GENES.411.1	hi-hi
	336924			CH.02, GENES.46.4	hi-hi
	335289			CH.02, GENES.527.2	hi-hi
	335290			CH.02, GENES.527.3	hi-hi
80	335873			CH.02, GENES.527.4	hi-hi
	337181			CH.02, GENES.570.2	hi-hi
	335889			CH.02, GENES.517.5 (name as BFH)	hi-hi

WO 02/098358

PCT/US02/17594

335910			CH22_FGENES.617_7	b-b4
335924			CH22_FGENES.619_11 (same as BFH5)	b-b4
335954			CH22_FGENES.683_3	b-b4
333124			CH22_FGENES.81_8	b-b4
332340	AP000692	Hs.129781	chromosome Z1 open reading frame 5	b-b4
130380	A1949359	Hs.143600	type I Golgi membrane protein	b-b4
102662	R50532	Hs.152563	collagen, type VI, alpha 2	b-b4
331506	AF102646	Hs.63531	dachshund (Drosophila) homolog	b-b4
319408	AA448090	Hs.87369	ESTs, Highly similar to R818 MOUSE RAS-R	b-b4
312197	T96203		gbya4807.r1 Soares fetal liver spleen	b-b4
312405	AI523875		gbya7004.x1 NCL_CGAP_C11 Homo sapiens	b-b4
312519	AA486930	Hs.24444	ESTs	b-b4
313475	AA010200	Hs.175551	ESTs	b-b4
313624	AA525775	Hs.250253	ESTs	b-b4
316897	AA838114	Hs.221612	ESTs	b-b4
317650	AB681545	Hs.152582	hypothetical protein FLJ15117	b-b4
318641	T50230	Hs.100715	ESTs	b-b4
321325	AB033100	Hs.300548	KIAA protein (similar to mouse poldin)	b-b4
321696	AA628791	Hs.78228	amplified in osteosarcoma	b-b4
322189	H65014		gbya5910.r1 Weizmann Olfactory Epithel	b-b4
323463	A1247564	Hs.137306	ESTs	b-b4
322540	R75553		gbya60u11.r1 Soares placenta NB2HP Homo	b-b4
323131	AK002088	Hs.270124	Homo sapiens cDNA FLJ11226 fs, clone PL	b-b4
323243	W47525	Hs.110771	Homo sapiens cDNA: FLJ21304 fs, clone H	b-b4
323381	AA512270		gbya51452 Testis larva Homo sapiens cD	b-b4
323753	AK002161	Hs.70266	yeast Sec3p1 homolog	b-b4
323836	AL042006	Hs.1117	lipidyltransferase II	b-b4
323926	AA354572		gbya52857 perlecan T-cells V Homo sapien	b-b4
324047	AA33357	Hs.271340	ESTs	b-b4
324330	AA84793		gbya2010u1 Soares NHL_T_GDC_S1 Homo s	b-b4
324753	AA612826	Hs.144871	Homo sapiens cDNA FLJ13752 fs, clone PL	b-b4
300702	AA075481	Hs.111334	tannin, light polypeptide	b-b4
301712	BE063080	Hs.274323	Homo sapiens. Similar to siayltransfera	b-b4
302380	AA325533	Hs.136102	KIAA0853 protein	b-b4
302570	W05698	Hs.312579	EST	b-b4
303187	AA115952	Hs.323423	ESTs, Moderately similar to B Chain B,	b-b4
303194	AA082000		gbya26107.r1 Stratagene neuroepithelium	b-b4
306612	AA782347	Hs.272572	hemoglobin, alpha 2	b-b4
304253	AA028837		gbya2611u1 Stratagene connective tissue	b-b4
304275	AA070905		gbya2610u1 Stratagene fibroblast (S37	b-b4
304309	AA112147		gbya2610u1 Stratagene fibroblast (S37	b-b4
305603	AA739177	Hs.238148	ESTs, Weakly similar to KIAA0655 protei	b-b4
308615	AA020142	Hs.101774	hypothetical protein FLJ23045	b-b4
309390	AIW08695		gbya3308.x1 NCL_CGAP_Co18 Homo sapiens	b-b4
104657	A123923	Hs.30098	ESTs	b-b4
310014	D60745	Hs.23525	Homo sapiens clone 23890 mRNA sequence	b-b4
310814	W07351	Hs.22545	Homo sapiens cDNA FLJ12935 fs, clone NT	b-b4
311858	CD4893	Hs.47191	ESTs	b-b4
311651	W52448	Hs.58147	ESTs	b-b4
332120	AA069994	Hs.112748	Homo sapiens cDNA: FLJ21543 fs, clone C	b-b4
332228	AA937608	Hs.102754	ESTs	b-b4
107252	D60745	Hs.23525	Homo sapiens clone 23890 mRNA sequence	b-b4
112058	AA264847	Hs.22545	Homo sapiens cDNA FLJ12935 fs, clone NT	b-b4
117929	N51075	Hs.47191	ESTs	b-b4
118537	W52448	Hs.58147	ESTs	b-b4
123712	AA069994	Hs.112748	Homo sapiens cDNA: FLJ21543 fs, clone C	b-b4
124580	AA937608	Hs.102754	ESTs	b-b4
106039	AA907305	Hs.36475	ESTs	b-b4
106271	AA807881	Hs.25323	ESTs	b-b4
106589	AA259584	Hs.237372	ESTs	b-b4
105646	AI137281	Hs.17110	Homo sapiens mRNA: cDNA DKFZp434C2016 f	b-b4
107071	AIW385224	Hs.35198	ectonucleoside triphosphate phosphodi	b-b4
108218	W57550	Hs.501526	hypothetical protein FLJ15181	b-b4
110930	BE242891	Hs.14347	ESTs, Weakly similar to ALU1_HUMAN ALU S	b-b4
112596	RA4714	Hs.105795	Homo sapiens cDNA FLJ15126 fs, clone NT	b-b4
112170	BE248743	Hs.295629	hypothetical protein FLJ22638	b-b4
112902	AL035633	Hs.129190	Human DNA sequence from clone RPS-1046C1	b-b4
114877	AW024162	Hs.205125	ESTs	b-b4
116312	BE379794	Hs.65403	hypothetical protein	b-b4
116738	H01463	Hs.33534	ESTs	b-b4
119267	AA064970	Hs.118145	ESTs	b-b4
120570	AA280579	Hs.271445	ESTs, Weakly similar to ALU1_HUMAN ALU	b-b4
121176	AL121523	Hs.39774	ESTs	b-b4
123360	AA532718	Hs.178604	ESTs	b-b4
123974	NHL015878	Hs.3821	neuridecin	b-b4
124077	RA1933		gbya4009.s1 Soares infant brain T1818	b-b4
128046	AA873285		gbya6890.s1 NCL_CGAP_KJ65 Homo sapiens	b-b4
128696	AA305446	Hs.103395	hypothetical protein FLJ14145	b-b4
130839	AA57212	Hs.171522	ESTs	b-b4
130933	R89537	Hs.17392	ESTs	b-b4
131756	AA443966	Hs.31595	ESTs	b-b4
131985	AA503020	Hs.35563	hypothetical protein FLJ22418	b-b4

WO 02/098358

PCT/US02/17594

132932	AW118828	Hs.6093	Homo sapiens cDNA, FLJ22783 fls, clone K	to-hi-to
134098	BC326276	Hs.6881	ESTs	to-hi-to
300967	AA565209	Hs.269430	ESTs	to-hi-to
301182	AW291411	Hs.192531	ESTs, Weakly similar to 500754 zinc finger	to-hi-to
302895	AB693372	Hs.193247	Homo sapiens mRNA; cDNA DKF-Zp43A171 (tr	to-hi-to
331152	A929819	Hs.4355	chromosome 21 open reading frame 50	to-hi-to
303046	AA348405	Hs.105887	ESTs, Weakly similar to Homolog of rat Z	to-hi-to
303654	BE246743	Hs.288529	hypothetical protein FLJ22635	to-hi-to
310026	AA278233	Hs.100691	ESTs	to-hi-to
310066	A253072	Hs.143383	ESTs	to-hi-to
310353	A261710	Hs.145544	ESTs	to-hi-to
310371	A282584	Hs.145575	ESTs	to-hi-to
310430	A1670843	Hs.200257	ESTs	to-hi-to
310438	AW022192	Hs.220187	ESTs	to-hi-to
310455	A1277653	Hs.145980	ESTs	to-hi-to
310787	AW263280	Hs.147874	KIAA1621 protein	to-hi-to
311067	AB587332	Hs.229115	ESTs	to-hi-to
311422	F00677	Hs.101316	ESTs	to-hi-to
311465	A738660	Hs.206132	ESTs	to-hi-to
312073	AA482393	*Hs.116527	ESTs	to-hi-to
312105	T81819	Hs.302251	ESTs	to-hi-to
312108	T82331	*Hs.127453	ESTs	to-hi-to
312292	AW450103	Hs.151124	ESTs	to-hi-to
312313	AW563341	Hs.122835	ESTs, Weakly similar to I38022 hypothetical	to-hi-to
312800	AW070805	Hs.204963	ESTs	to-hi-to
312800	A248774	Hs.129707	hypothetical protein FLJ11457	to-hi-to
312821	AA699325	Hs.269880	ESTs	to-hi-to
313067	AB76184	Hs.204339	ESTs	to-hi-to
313190	AA801098	Hs.151600	ESTs	to-hi-to
313179	AA627670	Hs.131704	ESTs	to-hi-to
313280	AW560454	Hs.222830	ESTs	to-hi-to
313669	AB08810	Hs.183288	ESTs	to-hi-to
314146	AB872237	Hs.282884	ESTs	to-hi-to
314305	AB291112	Hs.128232	Homo sapiens cDNA FLJ13256 fls, clone OV	to-hi-to
314465	AB879331	Hs.184595	ESTs	to-hi-to
314465	AA802917	Hs.156974	ESTs	to-hi-to
314681	AB095087	Hs.152229	ESTs, Moderately similar to ALUS_HUMAN A	to-hi-to
314618	AA548936	Hs.122244	ESTs	to-hi-to
315043	AA806538	Hs.130732	KIAA1575 protein	to-hi-to
315074	AA828284	Hs.136729	Homo sapiens cDNA: FLJ21348 fls, clone C	to-hi-to
315214	AB156227	Hs.34771	ESTs	to-hi-to
315314	AW252176	Hs.246834	ESTs	to-hi-to
315353	AS272949	Hs.278510	hypothetical protein FLJ10493	to-hi-to
315439	T78413	Hs.283698	ESTs	to-hi-to
315628	R37257	Hs.184780	ESTs	to-hi-to
315720	AA282898	Hs.163900	ESTs	to-hi-to
315772	AW153773	Hs.271246	Homo sapiens cDNA FLJ13580 fls, clone PL	to-hi-to
315841	AW138397	Hs.247572	ESTs	to-hi-to
316042	AA689980	Hs.170998	ESTs	to-hi-to
316244	AB410781	Hs.224988	ESTs	to-hi-to
316345	AW159408	Hs.153940	ESTs	to-hi-to
316825	BE540050	Hs.122156	ESTs	to-hi-to
316738	AA889056	Hs.123488	ESTs	to-hi-to
316808	AB60888	Hs.195002	ESTs	to-hi-to
316905	AW158241	Hs.210846	ESTs	to-hi-to
317224	T73638	*Hs.33029	spandactinectin, ewc and kazal-like d	to-hi-to
317275	AB034444	Hs.202108	ESTs	to-hi-to
317404	AB068667	Hs.128594	ESTs	to-hi-to
317488	AW071801	Hs.130628	ESTs	to-hi-to
317916	AB565071	Hs.159965	ESTs	to-hi-to
317959	AB952208	Hs.244760	ESTs	to-hi-to
318486	T23514		gbseq3329 1-NB Homo sapiens cDNA clone	to-hi-to
319897	NA6874	Hs.43838	ESTs	to-hi-to
320654	AI160015	Hs.118112	ESTs	to-hi-to
320697	BE25137	Hs.269109	ESTs	to-hi-to
320787	AW088363	Hs.246240	ESTs	to-hi-to
321023	AW294316	Hs.125608	ESTs	to-hi-to
321899	AW872832	Hs.29468	ESTs	to-hi-to
322639	AA101687	Hs.211270	ESTs	to-hi-to
323045	AA148950	Hs.188836	ESTs	to-hi-to
323091	AB02456	Hs.210761	ESTs	to-hi-to
322652	AL133990	Hs.190642	ESTs	to-hi-to
323410	AW118893	Hs.194150	ESTs	to-hi-to
323645	AW445014	Hs.197746	ESTs	to-hi-to
324598	AW872227	Hs.163396	Homo sapiens cDNA: FLJ22765 fls, clone K	to-hi-to
324666	T76413	Hs.283696	ESTs	to-hi-to
324874	AA541323	Hs.118831	ESTs	to-hi-to
324713	AB063930	*Hs.213466	ESTs	to-hi-to
324790	AI334367	Hs.159337	ESTs	to-hi-to
324804	AB925652		gbwdf3812.x1 NC_CGAP_Lu24 Homo sapiens	to-hi-to
330728	AB056520	Hs.28672	ESTs	to-hi-to
330780	H04988	Hs.30469	ESTs	to-hi-to

WO 02/098358

PCT/US02/17594

	330776	AW953805	Hs.21887	ESTs	to-Hs-Hs
	330824	AB037732	Hs.61441	KIAA1311 protein	to-Hs-Hs
	331028	AB319521	Hs.28338	KIAA1545 protein	to-Hs-Hs
5	331046	N68563	Hs.191358	ESTs	to-Hs-Hs
	331050	BE007987	Hs.155795	ESTs	to-Hs-Hs
	331053	AI949841	Hs.183146	ESTs, Moderately similar to ALU1_HUMAN A	to-Hs-Hs
	331180	U46892	Hs.6640	Human DNA sequence from PAC 78N13 on chr	to-Hs-Hs
	331313	A2751094	*Hs.30818	hypothetical protein	to-Hs-Hs
10	331337	N74392	Hs.50495	ESTs	to-Hs-Hs
	331393	AW978438	*Hs.17428	RBP1-like protein	to-Hs-Hs
	331432	AA252451	Hs.38485	ESTs	to-Hs-Hs
	331517	AA785603	Hs.163677	H3 histone, family 3D (H3.3E)	to-Hs-Hs
	331686	AW474980	Hs.182258	ESTs	to-Hs-Hs
15	332002	A057909	Hs.105104	ESTs	to-Hs-Hs
	332043	AA571307	Hs.125056	ESTs	to-Hs-Hs
	332295	AW70320	Hs.222413	ESTs	to-Hs-Hs
	332314	RA1396	Hs.101774	hypothetical protein FLJ23045	to-Hs-Hs
	131517	AB037789	Hs.263395	ozma domain, transmembrane domain (TM),	to-Hs-Hs
	131562	AA604799	Hs.138528	ESTs, Moderately similar to ALU1_HUMAN A	to-Hs-Hs
	131548	AA628539	Hs.118252	ESTs, Moderately similar to ALU1_HUMAN A	to-Hs-Hs
	321489	AA691177	Hs.172709	ESTs, Moderately similar to ALU1_HUMAN A	to-Hs-Hs
	108909	NM_012068	Hs.9754	activating transcription factor 5	to-Hs-Hs
	105726	NM_012068	Hs.9754	activating transcription factor 5	to-Hs-Hs
25	131925	AB207019	Hs.154652	DnaI (tsp40) homolog, subfamily A, membe	to-Hs-Hs
	1314915	AB573735	Hs.187748	ESTs, Weakly similar to ALU1_HUMAN ALU S	to-Hs-Hs
	1315198	AA741505	Hs.198763	ESTs, Weakly similar to ALU1_HUMAN ALU S	to-Hs-Hs
	324302	AF1972771	Hs.292471	ESTs, Weakly similar to ALU1_HUMAN ALU S	to-Hs-Hs
	331341	BE541042	*Hs.23240	Home sapiens cDNA FLJ13496 fs, clone PL	to-Hs-Hs
30	113763	AL358588	Hs.7041	hypothetical protein DKFZp762B226	to-Hs-Hs
	131552	AB893208	Hs.17283	hypothetical protein FLJ10890	to-Hs-Hs
	103698	AA315593	Hs.155494	Home sapiens regenerating gene type IV m	to-Hs-Hs
	331492	AK001114	Hs.63913	hypothetical protein FLJ10252	to-Hs-Hs
	110837	H03109	Hs.108920	HT018 protein	to-Hs-Hs
35	330814	AB95040	Hs.265398	ESTs, Weakly similar to transformation-r	to-Hs-Hs
	131228	AA315703	Hs.199953	ESTs	to-Hs-Hs
	102034	AI903474	Hs.230	fibronectin	to-Hs-Hs
	134671	BE283255	Hs.302749	FK506-binding protein 9 (53 kD)	to-Hs-Hs
	131063	Y09763	Hs.22785	gamma-aminobutylic acid (GABA) A recepto	to-Hs-Hs
40	309575	AI116808	Hs.165478	glycerol(1,3)-3-phosphate dehydrogenase	to-Hs-Hs
	134332	DB8962	Hs.81875	growth factor receptor-bound protein 10	to-Hs-Hs
	132904	NM_005518	Hs.59889	3-hydroxy-3-methylglutaryl-Coenzyme A sy	to-Hs-Hs
	302910	N77976	Hs.251577	hemoglobin, alpha 1	to-Hs-Hs
	133781	N71725	*Hs.272572	hemoglobin, alpha 2	to-Hs-Hs
45	333297	AF072623	Hs.19423	Home sapiens clone 24468 mRNA sequence	to-Hs-Hs
	108732	AA258888	Hs.167476	ATP synthase, H+ transporting, mitochond	to-Hs-Hs
	108731	AA258888	Hs.107476	ATP synthase, H+ transporting, mitochond	to-Hs-Hs
	302723	AB015452	Hs.148931	ATFase, aminophospholipid transporter (A	to-Hs-Hs
	131614	AB002438	Hs.29591	Home sapiens mRNA from chromosome Sq2-2	to-Hs-Hs
50	104033	N64128	Hs.12969	hypothetical protein	to-Hs-Hs
	302235	AL049887	Hs.188381	Home sapiens mRNA; cDNA DKFZp594F112 (fr	to-Hs-Hs
	320574	AL049443	Hs.161283	Home sapiens mRNA; cDNA DKFZp598N2020 (fr	to-Hs-Hs
	324678	AB950739	Hs.77868	CRP	to-Hs-Hs
	331822	H03109	Hs.108920	HT018 protein	to-Hs-Hs
	332430	H25350	Hs.21146	hypothetical protein FLJ22469	to-Hs-Hs
55	330601	U09916	Hs.82845	Home sapiens cDNA: FLJ21930 fs, clone H	to-Hs-Hs
	101988	AF221521	Hs.8068	hematopoietic PBX-interacting protein	to-Hs-Hs
	102659	AL038568	*Hs.76807	major histocompatibility complex, class	to-Hs-Hs
	101383	M11321			to-Hs-Hs
60	133968	AA355896	Hs.232068	transcription factor 8 (represses initial	to-Hs-Hs
	332530	M31669	Hs.1735	inhibin, beta B (activin AB beta polypep	to-Hs-Hs
	131777	NM_014785	Hs.47313	KIAA0238 gene product	to-Hs-Hs
	100452	DB7742	Hs.241552	KIAA0263 protein	to-Hs-Hs
	112988	NM_014867	Hs.5333	KIAA0711 gene product	to-Hs-Hs
	320848	AB026681	Hs.198232	KIAA0884 protein	to-Hs-Hs
65	109162	AL133033	*Hs.4084	KIAA1025 protein	to-Hs-Hs
	133805	AB026974	Hs.157478	KIAA1051 protein	to-Hs-Hs
	331406	BE178953	Hs.23440	KIAA1105 protein	to-Hs-Hs
	321441	AF107493	Hs.118498	Home sapiens LUC1A-15 protein mRNA, splic	to-Hs-Hs
70	131913	AW207440	Hs.185973	degenerative spinalnucleo (homolog Dros	to-Hs-Hs
	135424	U67611		transaldolase 1	to-Hs-Hs
	128595	L4804	Hs.100724	protonome proliferative activated oncop	to-Hs-Hs
	330596	AI130740	Hs.6241	phosphoinositide-3-kinase, regulatory su	to-Hs-Hs
	311251	AB626862	Hs.197989	ESTs	to-Hs-Hs
75	1314171	AB21895	Hs.193481	ESTs	to-Hs-Hs
	108096	AW197879	Hs.176121	protein tyrosine phosphatase, receptor t	to-Hs-Hs
	133740	AW192919	*Hs.170150	RAB2, member RAS oncogene family-like	to-Hs-Hs
	119521	W36038			to-Hs-Hs
	119548	W38189			to-Hs-Hs
80	119559	W38197			to-Hs-Hs
	133797	AL153621	Hs.76272	reticuloblastoma-binding protein 2	to-Hs-Hs
	305096	AA642964	Hs.163593	ribosomal protein L18a	to-Hs-Hs
	120255	AA169801	Hs.98710	hypothetical protein	to-Hs-Hs

WO 02/098358

PCT/US02/17594

5	322919	AA178958	Hs.271439	ESTs	to-Ho-3o
	300595	RS4326	Hs.328502	son of sevenless (Drosophila) homolog 1	to-Ho-3o
	330694	AT741817	Hs.108447	glucosaminidase 7 (oligosaccharose	to-Ho-3o
	302416	AL120259	Hs.76891	stannin	to-Ho-3o
	319289	AA037534	Hs.79059	transforming growth factor, beta receptor	to-Ho-3o
10	134866	AT700878	Hs.67409	thrombospondin 1	to-Ho-3o
	130117	U06541	Hs.150207	UDP-glycosyltransferase 2 family, polype	to-Ho-3o
	124357	N22401		gbyru5/g07.s1 Morton Fetal Cochlea Homo	to-Ho-3o
	106295	AA069155		glc2m10f1.s1 Stratagene pancreas (93720	to-Ho-3o
	108657	BE557533	Hs.132955	BCL21adenovirus E1B 19kD-interacting pro	to-Ho-3o
15	106541	AA641496		gbcz6f10.s1 NCL-COPX_Lympho Homo sapiens	to-Ho-3o
	331278	AA071183		gbcz6f10.s1 Stratagene fibroblast (937	to-Ho-3o
	106340	AA069820	Hs.180909	peroxiredoxin 1	to-Ho-3o
	108679	AA115963	Hs.323423	ESTs, Moderately similar to B Chain B,	to-Ho-3o
	108406	AA075424	Hs.325505	ESTs, Moderately similar to FBA_HUMAN HE	to-Ho-3o
20	114536	AA073981		gbczm5f0.s1 Stratagene ovarian cancer	to-Ho-3o
	108462	AA079347		gbczm5f0.s1 Stratagene colon HT29 (937	to-Ho-3o
	108465	AA079409		gbczm5f0.s1 Stratagene colon HT29 (937	to-Ho-3o
	108469	AA082937		gbczm7f10.s1 Stratagene hNT neuron (937	to-Ho-3o
	330359	AA028977		gbczm7f10.s1 Stratagene hNT neuron (937	to-Ho-3o
25	108505	AA053376		gbczm7f10.s1 Stratagene hNT neuron (937	to-Ho-3o
	331263	AA467736	Hs.278437	ESTs	to-Ho-3o
	100691	AW068302	Hs.162163	Homo sapiens mRNA for caldesmon, 3' UTR	to-Ho-3o
	106642	AW068302	Hs.162163	Homo sapiens mRNA for caldesmon, 3' UTR	to-Ho-3o
	326955			CH15_hs_g0505787	to-Ho-3o
30	338316			CH22_ENAAC005500.GENSCAN.149-6	to-Ho-3o
	100599	I38765	Hs.60706	CH22_ENAAC005500.GENSCAN.304-2	to-Ho-3o
	331131	RS4797		diaphorase (NADH:NADPH) (cytochrome b-5	to-Ho-3o
	130963	AA076732	Hs.263182	gbyr5707.s1 Scores infant brain HWB H	to-Ho-3o
	311137	AW027952	Hs.190542	ESTs	to-Ho-3o
35	311596	AW025595	Hs.232048	ESTs	to-Ho-3o
	313070	AA022223	Hs.161336	ESTs	to-Ho-3o
	110544	AT740792	Hs.167531	methylcrotonyl-Coenzyme A carboxylase 2	to-Ho-3o
	120328	AA923278	Hs.290905	ESTs, Weakly similar to protease [Hsapi	to-Ho-3o
	105914	AW024580	Hs.9701	growth arrest and DNA-damage-inducible,	to-Ho-3o
40	123509	NM_012446	Hs.281126	spondin 2, extracellular matrix protein	to-Ho-3o
	102759	NM_005100	Hs.765	A kinase (PRK) anchor protein (gavin)	to-Ho-3o
	100168	H73444	Hs.594	adrenomedullin	to-Ho-3o
	102346	U37519	Hs.87539	aldehyde dehydrogenase 6	to-Ho-3o
	134158	U15174	Hs.79428	BCL2adenovirus E1B 19kD-interacting pro	to-Ho-3o
45	133962	AUC78520	Hs.325474	caldesmon 1	to-Ho-3o
	101683	AUC78743	Hs.75613	CDS8 antigen (collagen type I receptor,	to-Ho-3o
	327621			CH1_05_hs_g0587966	to-Ho-3o
	134133	AA262294	Hs.160383	dual specificity phosphatase 6	to-Ho-3o
	103000	NM_0011975	Hs.146560	enkease 2, (gamma, neurone)	to-Ho-3o
50	106251	AA194718	Hs.63955	EST	to-Ho-3o
	315566	ABC37610	Hs.18780	KIAA1389 protein	to-Ho-3o
	324697	AK000742	Hs.128774	L2DT1 protein	to-Ho-3o
	306011	AA598968		gbcz06f0.s1 Borehead spleen HPLR82 Hom	to-Ho-3o
	307111	A174628		gbcz05f10.s1 Genetec Wilms tumor Homo s	to-Ho-3o
55	106839	AV055272	Hs.20252	novel Ras family protein	to-Ho-3o
	106753	AV056166	Hs.7331	hypothetical protein FLJ22316	to-Ho-3o
	107974	AV0568103	Hs.61712	pyruvate dehydrogenase kinase, isoenzyme	to-Ho-3o
	112333	RH9031	Hs.22827	ESTs	to-Ho-3o
	115616	I46506	Hs.31510	ESTs	to-Ho-3o
60	118024	AA069767	Hs.83883	transmembrane, prostate androgen induced	to-Ho-3o
	118150	AA381607	Hs.61782	hypoxia-inducible protein 2	to-Ho-3o
	119071	R31160		glycyl-h2b2.s1 Scores placenta Nb2HP Homo	to-Ho-3o
	120132	W57564	Hs.126019	ESTs	to-Ho-3o
	120652	AA305599	Hs.235205	hypothetical protein PRC2C13	to-Ho-3o
65	122411	AW172356	Hs.96063	ESTs	to-Ho-3o
	320778	AA615354	Hs.169696	ESTs	to-Ho-3o
	321024	AW048215	Hs.32058	Homo sapiens C1orf119 mRNA, partial cds	to-Ho-3o
	321408	AW061530	Hs.137088	ESTs, Weakly similar to ALU1_HUMAN ALU S	to-Ho-3o
	323620	AA306997	Hs.265382	ESTs, Weakly similar to hypothetical pro	to-Ho-3o
70	314946	AW097229	Hs.217464	ESTs	to-Ho-3o
	320653	AA334511	Hs.26538	ESTs, Weakly similar to unnamed protein	to-Ho-3o
	122699	AS60127	Hs.407361	hypothetical protein FLJ11200	to-Ho-3o
	126892	TS3025	Hs.107	Rimogroup-like 1	to-Ho-3o
	133592	AV052095	Hs.75113	general transcription factor IIIA	to-Ho-3o
75	103245	BE566343	Hs.28988	glutaredoxin (thioltransferase)	to-Ho-3o
	314785	AS335226	Hs.32976	guanine nucleotide binding protein 4	to-Ho-3o
	103677	Z53606		gblt3.sapiens mRNA for axonemal dydin ho	to-Ho-3o
	131710	NM_014283	Hs.23796	ozd (odd Cytos-m, Drosophila) homolog 1	to-Ho-3o
	311164	AW013807	Hs.182265	keratin 19	to-Ho-3o
80	100429	D68957	Hs.60712	KIAA0272 protein	to-Ho-3o
	133157	AW162840	Hs.88414	kinasin family member 5C	to-Ho-3o
	319080	AW067545	Hs.23023	ESTs	to-Ho-3o
	330706	AF097994	Hs.301528	L-lysine/alpha-aminoadipate aminotra	to-Ho-3o
	104082	NM_002407	Hs.97944	mammaglobin 2	to-Ho-3o
	100647	MS7417		gblt3.sapiens mchm (mucin) mRNA, part	to-Ho-3o

WO 02/098358

PCT/US02/17594

	103145	X68276	Hs.169849	myosin-binding protein C, slow-type	lo-to-hi
	301015	AV853272	Hs.20252	novel Ras family protein	lo-to-hi
	311013	AJ224760	*Hs.153	ribosomal protein L7	lo-to-hi
	132050	A26787.5	Hs.38022	ESR1	lo-to-hi
5	132349	AW975654	*Hs.181286	serine protease inhibitor, Kazal type 1	lo-to-hi
	130889	AW972612	Hs.20985	sin3-associated polypeptide, 30KD	lo-to-hi
	130791	AF030403	Hs.199263	Ste-20 related kinase	lo-to-hi
	130385	AW967800	Hs.155223	stardustcoklin 2	lo-to-hi
10	172729	AA316181	Hs.61635	six transmembrane epithelial antigen of	lo-to-hi
	133820	S96881	*Hs.177582	surfactant, pulmonary-associated protein	lo-to-hi
	129523	M13231	Hs.274509	T cell receptor gamma constant 2	lo-to-hi
	321415	DS921807	Hs.3337	transmembrane 4 superfamily member 1	lo-to-hi
	131859	AW960564	*Hs.5337	transmembrane 4 superfamily member 1	lo-to-hi
15	133444	M63978	Hs.73793	vascular endothelial growth factor	lo-to-hi
	332567	AW939251	*Hs.25647	v-fos FBJ murine osteosarcoma viral onco	lo-to-hi
	131328	AW939251	*Hs.25647	v-fos FBJ murine osteosarcoma viral onco	lo-to-hi
	316901	AI921559	Hs.7331	hypothetical protein FLJ22316	lo-to-hi
	104394	AA129551	Hs.172120	Homo sapiens cDNA: FLJ21409 lit, clone C	lo-to-hi
20	103739	AA115173		gpczn30002.z1 Stratagene neuroepithelium	lo-to-hi
	103797	AA080912		gpczn04003.r1 Stratagene HNT neuron (337	lo-to-hi
	103804	AA129196		gpczn29009.r1 Stratagene neuroepithelium	lo-to-hi

PCT/US02/17594

H03029 N7701 AW151751 H00925 AW45583 H72947 NB8334 N55487 AI259891 AA581634 AV651323 AV8551728 AV850086 AV861295
AV940842 AW026000 AW537887 AA249713 AW080241 H73463 AW471335 AW150316 AA360851 W01407 DE074001 W21371 T27221
AA156991 D16905 AW862400 AW651466 AI587816 AA442743 AI189898 AW887793 BE005206 AW860165 AW317024 AA976151 AA247314
AT671814 RE4644 RE2817 D57595 N74437 H74383 H80409 N66050 H91165 R79462 F09991 R26175 H77253 N25250 D56667 AA473616
D56666 D56903 AW21855 AW347084 RE43794 H66894 T81638 T63365 W23835 R67668 AW201682 H81164 H61939 H88988 AW26106 W25710

WO 02/098358

PTC/US2021/7594

WA2696 AA38428 AW994316 HB5163 HB5158 B23688 WA6557 AW740451 AA028916 AA463026 AA314207 B23204 AA338891 HD2026
AA104566 HB3632 C03297 BE3741 HB4533 B23228 B04618 HA4620 AA03671 AA343386 HA4204 B026181 AA331313
B21710 B00701 T04222 BE1250 HA6336 B02779 AA579734 BE4111 AA344527 AB05473 B66666 B20056 T52284 AA10303 B20512 B21874
B13363 AA220933 BE439695 AA186983 AA164801 AA330833 AA788249 AA42361 W02687 AA303316 AW952009 AA343544 AA076799
AA16170 B70338 AA039612 AW92489 AA044620 AA353203 AA043082 AB68616 AW128024 AW195268 AA136106 AA447326 AA034801
AA032220 B20258 AA053279 B23239 AB056789 BE44557 AB00892 AA150016 BE46303 AA030369 AA030352 AA125887 AW68134
AA33047 AA195309 AW950489 AA454347 AA129657 AA870381 AA460202 H01227 W02579 B06049 B06524 AA00855 AA2271 BE139450
HA42228 H07671 AA161080 AD04361 AD052767 AB474165 AA688106 AA056879 B79463 AA029917 B06637 AB10134 AA046820 AA337796
AD14370 AA54637 AA620549 AA664223 AD062196 AA080303 AD014004 AB03165 AA300504 A1E7269 AA533851 H01743 AA103102
AW333971 YU42947 WA65106 AA143210 AA024745 AA417906 AA219359 AW466142 HB7699 A1B0616 AA315137 AA03375 A1B0320 1B8119
HB513 AL040481 AB28116 BE3701 B21712 B23686 AB11274 AB183274 AA1473300 AA019282 B037339 AB019282 B037339 AB019282
AA14370 AB43907 AA032271 AA182271 B21712 B21940 HB3633 AB089339 C75673 A0251394 AA614765 AW463007 A0251426 W03148 AW023141
AD72631 B79725 AA346566 C06197 127764 HB5138 AB14916 AA465299 AD119227 AB067672 B07090 A192026 B217134 AA067442
HB0916 AB025648 AA01868 AD120069 AB032668 AB688728 AA196395 B23334 B23271 B23280 AB06697 B24538 AB06697 B156374
B27795 B11162 AA371400 AB062126 AA0422253 F53323 AB042337 AB023617 H27442 AA039729 AA330303 A150704 AA04304 A2175779
AA747616 AB32269 B02395 HA4458 B25116 AB21869 AA164532 BE146079 B00002 AA033471 AA070506 AA187742 B07196 B22738 B33544
AD17181 B07005 AD24311 HB1590 AB060796 BE129244 B33654 B06850 AB194385 AA687691 HB0013 AA002001 AA054480 AA005734
AW068302 A1745658 AD750727 T052631 AA302174 AA327522 M54110 AW065944 AW065989 A175195 AA070620 AB08828 A292475
AB08836 AA042921 AB05060 AW080929 A1924908 AA063628 AB03900 AA519691 A025401 BE040740 AA34442 AA0138657 AA134330
AL046534 AB052865 AA001085 B03946 AW062528 W025261 AA042863 B09045 B079060 W03810 B04687 AB019807 A1924908 A2171566
AA04694 AB76879 AB063055 W02332 AA047379 AB142646 AA335387 AB1814748 AB303990 N7340 B03636 AL047816 A2171566 B23633
AA24384 AD234043 AA195131 B08903 AA45369 AD240302 AA320721 AB050026 A0071049 AA121476 AB069557 A1752862 A235594
AA471933 A15941 B4555 A1753138 B21537 HB7881 B125769 AW068044 AA080425 B63380 AA384736 AA384736 AB082332 AD073645
AA027980 AA025636 AA044414 A752460 AA073064 B01216 AA089713 AB11996 B1078 H05047 AA578342 B05846 B20053 AA134330
HB5148 AB47540 AB067596 AA07000 AB051901 AB067700 AA024241 AB27133 B20491 AA051891 AB029620 A024044 AA131039
AW994884 HB0619 AA994438 AA319216 AA319469 AA318727 AA318211 AA318478 AA31844 AA318307 AA31844 AA31843 AB131409
AA318496 AA318213 AA318424 AA318247 AA318523 AA318438 AA318487 AA318724 AA583185 AW069485 B6942 A251813
AA478174 AA042377 B18330 F0712 AA121146 H08733 AA345212 BE000667 AB068210 AW093407 B05674 H18712 B18426 HA2354
HB516 BE471991 B28113 B23662 AA384678 AW029275 BE2382 AB040700 C58229 C0462 WA534 AW175667 B79373 BE004049
AA042828 AB335355 A2232812 AA347019 BE145690 B70095 WA6881 W00716 N71242 AA345262 AL040676 B27197 B0640 AB062667
D79947 WA6950 AW068278 AA266997 AD026215 AW574969 AA365135 AA355143 AA3594363 AA597286 AW069161 AB03680 AB088731
A1751527 A493349 AB037006 AB026715 BE055400 A1925532 AB058109 AB058524 A2075201 BE005555 AL048166 AB0141 AB089221
AA375953 AA523181 AW068366 AW067789 AB071837 B0395 AW102753 AA222919 AB79733 BE005555 AL048166 AB0141 AB089221
A220443 B27827 AB0744 AA319128 AA0048 AB073247 HB616 HB624 AW06765 AB146800 AB072801 A475281 A170174 AW069022
AW069069 AW069454 AA324399 A007712 A3111467 AD07361 AB001015 WA6993 AB281324 AA1951963 A211575 A200861 A336670
AA871306 A1004219 AB189685 AA470816 AB070603 A1445222 A73124 A521569 AB05206 A022366 AB073991 B20046 A192046 A163123
A291710 B03442 AW11789 AB007935 A558975 AB00636 AB088963 AB05261 AB059355 AA462691 H10713 AB13383 AB0547712
A772521 A210928 B05433 AA03775 AW06810 AB06915 A1735291 AB08762 A210328 AB06851 WA0681 N22201 B22726 B16555
AA047447 AW040535 AW517756 AA069921 A007577 AW6216 A2155339 B06373 AA023948 C15961 B16001 A25145 AW069177
BE405090 A2173006 C16390 C16503 AD20823 C13661 B68664 Z21311 C16108 C16089 C16400 A0758273 A2187781 AA084878 A0208674
AA027380 AB052036 AA044414 A752460 AA073064 B01216 AB087183 AB11996 B1078 H05047 AA578342 B05846 B20053 AA437143
B05438 AA047540 AB067596 AA07000 AB051901 AB067700 AA024241 AB27133 B20491 AA051891 AB029620 A024044 AA131039
AA04694 AB76879 AB063055 W02332 AA047379 AB142646 AA335387 AB1814748 AB303990 N7340 B03636 AL047816 A2171566 B23633
A254494 AD234043 AA195131 B08903 AA45369 AD240302 AA320721 AB050026 A0071049 AA121476 AB069557 A1752862 A235594
AA471933 A15941 B4555 A1753138 B21537 HB7881 B125769 AW068044 AA080425 B63380 AA384736 AA384736 AB082332 AD073645
AA027380 AB052036 AA044414 A752460 AA073064 B01216 AB087183 AB11996 B1078 H05047 AA578342 B05846 B20053 AA437143
B05438 AA047540 AB067596 AA07000 AB051901 AB067700 AA024241 AB27133 B20491 AA051891 AB029620 A024044 AA131039
AA04694 AB76879 AB063055 W02332 AA047379 AB142646 AA335387 AB1814748 AB303990 N7340 B03636 AL047816 A2171566 B23633
A254494 AD234043 AA195131 B08903 AA45369 AD240302 AA320721 AB050026 A0071049 AA121476 AB069557 A1752862 A235594
AA471933 A15941 B4555 A1753138 B21537 HB7881 B125769 AW068044 AA080425 B63380 AA384736 AA384736 AB082332 AD073645
AA027380 AB052036 AA044414 A752460 AA073064 B01216 AB087183 AB11996 B1078 H05047 AA578342 B05846 B20053 AA437143
B05438 AA047540 AB067596 AA07000 AB051901 AB067700 AA024241 AB27133 B20491 AA051891 AB029620 A024044 AA131039
AA04694 AB76879 AB063055 W02332 AA047379 AB142646 AA335387 AB1814748 AB303990 N7340 B03636 AL047816 A2171566 B23633
A254494 AD234043 AA195131 B08903 AA45369 AD240302 AA320721 AB050026 A0071049 AA121476 AB069557 A1752862 A235594
AA471933 A15941 B4555 A1753138 B21537 HB7881 B125769 AW068044 AA080425 B63380 AA384736 AA384736 AB082332 AD073645
AA027380 AB052036 AA044414 A752460 AA073064 B01216 AB087183 AB11996 B1078 H05047 AA578342 B05846 B20053 AA437143
B05438 AA047540 AB067596 AA07000 AB051901 AB067700 AA024241 AB27133 B20491 AA051891 AB029620 A024044 AA131039
AA04694 AB76879 AB063055 W02332 AA047379 AB142646 AA335387 AB1814748 AB303990 N7340 B03636 AL047816 A2171566 B23633
A254494 AD234043 AA195131 B08903 AA45369 AD240302 AA320721 AB050026 A0071049 AA121476 AB069557 A1752862 A235594
AA471933 A15941 B4555 A1753138 B21537 HB7881 B125769 AW068044 AA080425 B63380 AA384736 AA384736 AB082332 AD073645
AA027380 AB052036 AA044414 A752460 AA073064 B01216 AB087183 AB11996 B1078 H05047 AA578342 B05846 B20053 AA437143
B05438 AA047540 AB067596 AA07000 AB051901 AB067700 AA024241 AB27133 B20491 AA051891 AB029620 A024044 AA131039
AA04694 AB76879 AB063055 W02332 AA047379 AB142646 AA335387 AB1814748 AB303990 N7340 B03636 AL047816 A2171566 B23633
A254494 AD234043 AA195131 B08903 AA45369 AD240302 AA320721 AB050026 A0071049 AA121476 AB069557 A1752862 A235594
AA471933 A15941 B4555 A1753138 B21537 HB7881 B125769 AW068044 AA080425 B63380 AA384736 AA384736 AB082332 AD073645
AA027380 AB052036 AA044414 A752460 AA073064 B01216 AB087183 AB11996 B1078 H05047 AA578342 B05846 B20053 AA437143
B05438 AA047540 AB067596 AA07000 AB051901 AB067700 AA024241 AB27133 B20491 AA051891 AB029620 A024044 AA131039
AA04694 AB76879 AB063055 W02332 AA047379 AB142646 AA335387 AB1814748 AB303990 N7340 B03636 AL047816 A2171566 B23633
A254494 AD234043 AA195131 B08903 AA45369 AD240302 AA320721 AB050026 A0071049 AA121476 AB069557 A1752862 A235594
AA471933 A15941 B4555 A1753138 B21537 HB7881 B125769 AW068044 AA080425 B63380 AA384736 AA384736 AB082332 AD073645
AA027380 AB052036 AA044414 A752460 AA073064 B01216 AB087183 AB11996 B1078 H05047 AA578342 B05846 B20053 AA437143
B05438 AA047540 AB067596 AA07000 AB051901 AB067700 AA024241 AB27133 B20491 AA051891 AB029620 A024044 AA131039
AA04694 AB76879 AB063055 W02332 AA047379 AB142646 AA335387 AB1814748 AB303990 N7340 B03636 AL047816 A2171566 B23633
A254494 AD234043 AA195131 B08903 AA45369 AD240302 AA320721 AB050026 A0071049 AA121476 AB069557 A1752862 A235594
AA471933 A15941 B4555 A1753138 B21537 HB7881 B125769 AW068044 AA080425 B63380 AA384736 AA384736 AB082332 AD073645
AA027380 AB052036 AA044414 A752460 AA073064 B01216 AB087183 AB11996 B1078 H05047 AA578342 B05846 B20053 AA437143
B05438 AA047540 AB067596 AA07000 AB051901 AB067700 AA024241 AB27133 B20491 AA051891 AB029620 A024044 AA131039
AA04694 AB76879 AB063055 W02332 AA047379 AB142646 AA335387 AB1814748 AB303990 N7340 B03636 AL047816 A2171566 B23633
A254494 AD234043 AA195131 B08903 AA45369 AD240302 AA320721 AB050026 A0071049 AA121476 AB069557 A1752862 A235594
AA471933 A15941 B4555 A1753138 B21537 HB7881 B125769 AW068044 AA080425 B63380 AA384736 AA384736 AB082332 AD073645
AA027380 AB052036 AA044414 A752460 AA073064 B01216 AB087183 AB11996 B1078 H05047 AA578342 B05846 B20053 AA437143
B05438 AA047540 AB067596 AA07000 AB051901 AB067700 AA024241 AB27133 B20491 AA051891 AB029620 A024044 AA131039
AA04694 AB76879 AB063055 W02332 AA047379 AB142646 AA335387 AB1814748 AB303990 N7340 B03636 AL047816 A2171566 B23633
A254494 AD234043 AA195131 B08903 AA45369 AD240302 AA320721 AB050026 A0071049 AA121476 AB069557 A1752862 A235594
AA471933 A15941 B4555 A1753138 B21537 HB7881 B125769 AW068044 AA080425 B63380 AA384736 AA384736 AB082332 AD073645
AA027380 AB052036 AA044414 A752460 AA073064 B01216 AB087183 AB11996 B1078 H05047 AA578342 B05846 B20053 AA437143
B05438 AA047540 AB067596 AA07000 AB051901 AB067700 AA024241 AB27133 B20491 AA051891 AB029620 A024044 AA131039
AA04694 AB76879 AB063055 W02332 AA047379 AB142646 AA335387 AB1814748 AB303990 N7340 B03636 AL047816 A2171566 B23633
A254494 AD234043 AA195131 B08903 AA45369 AD240302 AA320721 AB050026 A0071049 AA121476 AB069557 A1752862 A235594
AA471933 A15941 B4555 A1753138 B21537 HB7881 B125769 AW068044 AA080425 B63380 AA384736 AA384736 AB082332 AD073645
AA027380 AB052036 AA044414 A752460 AA073064 B01216 AB087183 AB11996 B1078 H05047 AA578342 B05846 B20053 AA437143
B05438 AA047540 AB067596 AA07000 AB051901 AB067700 AA024241 AB27133 B20491 AA051891 AB029620 A024044 AA131039
AA04694 AB76879 AB063055 W02332 AA047379 AB142646 AA335387 AB1814748 AB303990 N7340 B03636 AL047816 A2171566 B23633
A254494 AD234043 AA195131 B08903 AA45369 AD240302 AA320721 AB050026 A0071049 AA121476 AB069557 A1752862 A235594
AA471933 A15941 B4555 A1753138 B21537 HB7881 B125769 AW068044 AA080425 B63380 AA384736 AA384736 AB082332 AD073645
AA027380 AB052036 AA044414 A752460 AA073064 B01216 AB087183 AB11996 B1078 H05047 AA578342 B05846 B20053 AA437143
B05438 AA047540 AB067596 AA07000 AB051901 AB067700 AA024241 AB27133 B20491 AA051891 AB029620 A024044 AA131039
AA04694 AB76879 AB063055 W02332 AA047379 AB142646 AA335387 AB1814748 AB303990 N7340 B03636 AL047816 A2171566 B23633
A254494 AD234043 AA195131 B08903 AA45369 AD240302 AA320721 AB050026 A0071049 AA121476 AB069557 A1752862 A235594
AA471933 A15941 B4555 A1753138 B21537 HB7881 B125769 AW068044 AA080425 B63380 AA384736 AA384736 AB082332 AD073645
AA027380 AB052036 AA044414 A752460 AA073064 B01216 AB087183 AB11996 B1078 H05047 AA578342 B05846 B20053 AA437143
B05438 AA047540 AB067596 AA07000 AB051901 AB067700 AA024241 AB27133 B20491 AA051891 AB029620 A024044 AA131039
AA04694 AB76879 AB063055 W02332 AA047379 AB142646 AA335387 AB1814748 AB303990 N7340 B03636 AL047816 A2171566 B23633
A254494 AD234043 AA195131 B08903 AA45369 AD240302 AA320721 AB050026 A0071049 AA121476 AB069557 A1752862 A235594
AA471933 A15941 B4555 A1753138 B21537 HB7881 B125769 AW068044 AA080425 B63380 AA384736 AA384736 AB082332 AD073645
AA027380 AB052036 AA044414 A752460 AA073064 B01216 AB087183 AB11996 B1078 H05047 AA578342 B05846 B20053 AA437143
B05438 AA047540 AB067596 AA07000 AB051901 AB067700 AA024241 AB27133 B20491 AA051891 AB029620 A024044 AA131039
AA04694 AB76879 AB063055 W02332 AA047379 AB142646 AA335387 AB1814748 AB303990 N7340 B03636 AL047816 A2171566 B23633
A254494 AD234043 AA195131 B08903 AA45369 AD240302 AA320721 AB050026 A0071049 AA121476 AB069557 A1752862 A235594
AA471933 A15941 B4555 A1753138 B21537 HB7881 B125769 AW068044 AA080425 B63380 AA384736 AA384736 AB082332 AD073645
AA027380 AB052036 AA044414 A752460 AA073064 B01216 AB087183 AB11996 B1078 H05047 AA578342 B05846 B20053 AA437143
B05438 AA047540 AB067596 AA07000 AB051901 AB067700 AA024241 AB27133 B20491 AA051891 AB029620 A024044 AA131039
AA04694 AB76879 AB063055 W02332 AA047379 AB142646 AA335387 AB1814748 AB303990 N7340 B03636 AL047816 A2171566 B23633
A254494 AD234043 AA195131 B08903 AA45369 AD240302 AA320721 AB050026 A0071049 AA121476 AB069557 A1752862 A235594
AA471933 A15941 B4555 A1753138 B21537 HB7881 B125769 AW068044 AA080425 B63380 AA384736 AA384736 AB082332 AD073645
AA027380 AB052036 AA044414 A752460 AA073064 B01216 AB087183 AB11996 B1078 H05047 AA578342 B05846 B20053 AA437143
B05438 AA047540 AB067596 AA07000 AB051901 AB067700 AA024241 AB27133 B20491 AA051891 AB029620 A024044 AA131039
AA04694 AB76879 AB063055 W02332 AA047379 AB142646 AA335387 AB1814748 AB303990 N7340 B03636 AL047816 A2171566 B23633
A254494 AD234043 AA195131 B08903 AA45369 AD240302 AA320721 AB050026 A0071049 AA121476 AB069557 A1752862 A235594
AA471933 A15941 B4555 A1753138 B21537 HB7881 B125769 AW068044 AA080425 B63380 AA384736 AA384736 AB082332 AD073645
AA027380 AB052036 AA044414 A752460 AA073064 B01216 AB087183 AB11996 B1078 H05047 AA578342 B05846 B20053 AA437143
B05438 AA047540 AB067596 AA07000 AB051901 AB067700 AA024241 AB27133 B20491 AA051891 AB029620 A024044 AA131039
AA04694 AB76879 AB063055 W02332 AA047379 AB142646 AA335387 AB1814748 AB303990 N7340 B03636 AL047816 A2171566 B23633
A254494 AD234043 AA195131 B08903 AA45369 AD240302 AA320721 AB050026 A0071049 AA121476 AB069557 A1752862 A235594
AA471933 A15941 B4555 A1753138 B21537 HB7881 B125769 AW068044 AA080425 B63380 AA384736 AA384736 AB082332 AD073645
AA027380 AB052036 AA044414 A752460 AA073064 B01216 AB087183 AB11996 B1078 H05047 AA578342 B05846 B20053 AA437143
B05438 AA047540 AB067596 AA07000 AB051901 AB067700 AA024241 AB27133 B20491 AA051891 AB029620 A024044 AA131039
AA04694 AB76879 AB063055 W02332 AA047379 AB142646 AA335387 AB1814748 AB303990 N7340 B03636 AL047816 A2171566 B23633
A254494 AD234043 AA195131 B08903 AA45369 AD240302 AA320721 AB050026 A0071049 AA121476 AB069557 A1752862 A235594
AA471933 A15941 B4555 A1753138 B21537 HB7881 B125769 AW068044 AA080425 B63380 AA384736 AA384736 AB082332 AD073645
AA027380 AB052036 AA044414 A752460 AA073064 B01216 AB087183 AB11996 B1078 H05047 AA578342 B05846 B20053 AA437143
B05438 AA047540 AB067596 AA07000 AB051901 AB067700 AA024241 AB27133 B20491 AA051891 AB029620 A024044 AA131

WO 02/098358

PCT/JP2002/17594

5

124182

116312

100676

130760

116334

159140

1931

30310.1

116357

18555.1

130786

49038.3

109141

4042.1

191986

151761

18573.1

116574

1858.1

107974

86033.2

107977

99965.1

132050

90001.1

132057

27494.1

75

101332

25130.1

AWK2132Z AW20657 AW86400 AW367831 H25209 BE387236 AW0281317 BE253372 J00139 X00885 V00507 BE253513 BE260890
BE263555 BE391734 BE264538 AW209186 AW1129455 AW209186 AW1129455 AW209186 AW1129455 AW209186 AW1129455 AW209186 AW1129455
AW259557 AW184532 AW259442 AW189449 AW35691 NML_000731 AW447080 AW303097 HW431 AW129404 BE271333 W23800 AW142541
AA651836 AW858001 AW026548 AW361777 AW65122 AW359154 AW039319 AW423092 AW89383 AW262751 AW134941 AW13820 AW033995
AW067679 HW0705 AW230482 AW436168 AW159573 AW11920 AW382094 AW80434 AW131 AW042790 AW024376 AW070705 AA555100
W13657 AW061138 AW119234 AW423410 AW919237 AW050448 AW359006 AW421096 AW375347 AW354490 AW426588 HW0646 AW412091 W07757
AW470731 AW428708 BE263659 AW453389 AW061161 W12030 AW488081 AW307107 AW381013 AW420851 AW428309 HW0445 BE041100
W03282 AA544921 NE0189 AW01106 AA5519401 AA527654 AW039300 AA451790 AW170593 AW053451 AA633192 AW421794 AW104373
AA834961 AW027195 AW274416 AA646231
AW37471 AW511357 AW370447 AW368500 AW1125413 AW3491547 AW06212180 HW0118 W55827 AW243058 AW06303 AW070788 AW57972
AW37471 AW511357 AW370447 AW368500 AW1125413 AW3491547 AW06212180 HW0118 W55827 AW243058 AW06303 AW070788 AW57972
BE373794 NML_015929 AW20880 AW169445 AW304501 AW521819 AW218730 AW093112 AW1693022 AW31399 AW18132 AA554244 AA488980
AW571520 AW150181 AA555059 AW69445 AW304501 AW521819 AW218730 AW093112 AW1693022 AW31399 AW18132 AA554244 AA488980
AW014750 AW262564 AW056881 AW660697 AW277973 AW490494 AW627239 W17352 AW491057 AW189405 AW262562 AW056115 AW093053
AW057542
W02761 AW134153 AW0507 W02758 W12552 AW150806 AW069608 HW0678 W12951 AW4156567 W23438 W17777 W47975 AW563326 W50421
W01256 W7700 AW25274 AW116119 AW150520 W46471 W420053 W44355 W62622 W41819 AW151324 W23601 W27274 AW050383 AW023601
AW020233 AW496736 W1522445 AW191877 D65870 AW754285 AW88146 AA423511 AW139349 AW194835 AW1994830 AW1994830 W67577
C1794 W20474 AW039188 AW580570 BE174525 AW030101 AW150581 AW359556 AW150644 W47659 W61772 W46248 W19048 W330450 W474241
AW190369 AW40206 AW414284 AW125277 W8370 AW35353 W42511 AW33816 W23404 AW36747 AW058529 W25319 AW335923
W01775 W75533 R15348 AW0474 W7668 W60512 W3447 AW1850 AW4246 AW094480 W02651 R2137
AW379131 BE45804 AW02909 AW558701 W140490 AW61887 AW14887 AW64355 AW353691 AW131779 AW157947 AW126997 AW160913
AW174507 AW45187 AW04181 AW04837 NML_002056 AW075223 AW107802 W19787 AW1420373 R00119
AW030460 W05399 AW054447 AW36420 AW147211 AW147686 AW17590 AW491457 AW052059 AW137828 AW84506 AW4278 AW1978200
AW06917 AW03573
AW04403 AW09999 NML_012333 AW104402 AW251775 AW251558 AW82744 AW221232 AW3549 AW145038 AW30573 AW273805 AW330403
AW032232 AW15361 AW85774 AW26536 AW26859 AW587082 AW351439 AW02041 AW187340 AW270502 AW192761 AW101818 AW196899
AW130722 AW1597260 AW413004 AW36561 AW176905 AW448820 AW425415 AW116887 AW481184 AW442482 AW150717 AW332699 AW248878
AA25204 AW170675 AW035077 AW216857 AW544 AW02982 AW420454 AW15071755 AW170735 AW190735 AW032691 AW23778 AW19474
AA251075 W05575 AW339359 W65715 W44020 AW302918 AW111920 W65277 W06355 AA354228 AW195773 AW102070 AW054558 AW049471
AW04977 AW403132 AW532380 AW167014 AW367230 W3595609 W187900 W070061 W1676538 AW240076 AW68310 AW080661
BE458009 AW058966 AW065595 AW421959 W05308 AW050272 AW026807 AW420744 AW306448 AW182820 AW152045 BE221335
W026130 AW16216 W05094 W04117 AW364731 AW148694 AW055448 AW23627 AW17801 W65735 AW052710 AW037733 BE046221
AW17250 AW40519 AW35905 AW24200 AW03697 W08346 AW05097 W27235 AW051912 AW051912 AW05097 W08346 W24728
AW052107 W44571 W05469 AA525482 W44199
AF052702 W44755 W12122 W42165 W11814 W12194 W77827 W24836 AW080708 AW580725 R21670 BE18479 BE184810 W45293 AW6997485
AW528164 W47708 AW48616 W15613 AW76125 AW312310 AW031246 AW10171 W47709 AW62277 AW10699 AW021738 AW0300113 BE459270
W373509 AW071740 AW112386 AW030024 AW163735 W09430 AW35807 AW038638 AW058511 AA505205 AA04505 AW17010 W72580
AW044560 W48822 W4341637 W04605 W40370 AW340777 F03790 W42404 AW481253 W33674 W42404 AW481253 W33674 W42404 AW481253 W33674
W08071 W45455 AW117136
W080809 AW268119 AW0333617 W1510 AW383538 W39372 W39390 AW4216875 AW372415 AW36867 AW196840 AW0311066 AW165568
AW1389728 AW1473546 W02595 AA433847 AW210171 AW19390026 AW10667 BE348739 AW07223 W42526 AW15308 W06625 AW08370 W05113
AW167157 AW244659 AW143247 AW14882 AW43697 BE09247 AW19120 AW030907 AW02059 BE22116 AW191015 W03209 AW35972 W04611
W192409 AW024404 AW049057 AW162144 AW263595 W16361 BE092223 AW36247 BE061121 AW140041 BE011216 AW167111 W01192 BE1222
W154300 AW007768 AW101833 W03814 AW455584 W62420 AW094266 BE002869 W627009 AW3803 AW455584 W62420 AW30754 AW040464
AF142090 AW176879 AW1176413 AW116428
AW219691 AF153329 AW179167 AF070372 NML_006733 AW145766 AW157567 AW157567 AW157567 AW157567 AW157567 AW157567 AW157567 AW157567
AW371744 AW06936 W0704870 AW092028 AW177173 AW181842 BE090424 AW66341 AW243020 AW103151 AW54424 AW1168283 AW14854
AW075408 AW000977 AW137497 AW179455 AW074368 AW630744 AW789069 AW1701338 AW174752
AA369303 AW336228 AW1964485 BE362385 W33711 AA344040 AA304660 AW705526 W32795 AW193730 AW162116 AW162116 AW162116 AW162116
AW51230 W84481 AW421374 W40326 W358466 W52031 AW23131 AW560014 AW082527 AW052704 W1954847 AW105294 W055375
AW362285 AW062304 AF038451 NML_006408 AW336115 AW116628 AW060044 AW14225 AW07781 AW41627 BE07208 AW17093
W1941118 AW192795 AW075324 AW209537 AW34717 AW180637 AW151674 W1888294 AW190665 AW364247 AW083021 AW192548 AW002338
AW164754 AW418131 BE28325 AW373742 AW436796 AA099945 AW135787 AW049001 AW147938 AW130846 AW458457 BE076956 BE042940
AW278847 AW411069 AW027013 AW196790 AW08994 AW177270 AW1801054 AW526201 AW073291 AW343091 AW157454 AW282621 AW01784
AW026677 AW222681 AW07290 AW058911 AW00431 AW0511 AW41949 AW37861 AW456541 AW24282 AW070127 AW164543 AW1641
AW456596 AA442829 AW027943 AW027943 AW027943 AW130920 AW277236 AW55670 AW070336 W473028 AW125068 AW25024 W10106
AW219194 AW76991 AA383482 AW026030 W16786 AW182462 AW37173 AW1040152 AW187421 AW459656 AA45130 AW191840 AW258429
W020091 AW135808 AW067567 AW241562 AW199015 AW190785 AW187832 AA632103 W424494 AW152169 AW191014 AA558444
AW191883 AW051300 AW040184 AW473555 AW157574 AW431946 AW68303 AW66613 AW033636 AW17201 AW072488 AW551226 AA520375
AW23254 AW452809 AW143297 AW0065 AW063938 AW063938 AW063938 W42511 AW32122 AW09291 AW321226 AW254545 AW100867 AW428627
W24475 AW176575 AW455930 AW314206 AA316508 AW316508 AW307697 W0844413 AW314052 AW027524 AW24261 W354225 AW1815198
AW166169 BE070273 AW07505 AW310613 AW425228 AW314146 AW437001 AW307795 AW316233 AA314372 AW316967 AW315724 AW31423235
AW393341 AA245366 W06663 AW066072
W056133 AW430209 AW09047 AW14382 AW755910 AW276849 AW470075 AW376511 AW161466 W55811 AW161430 AW461981 AW1966104
AW093511 AW052305 W23840 BE352094
W181861 AW119012 AW005979 AW04306 AW194387 W69597
AW267515 AW147943 AW30796 AW12866 W64943 AW150280 BE030091 AW022945 AW0332 W42731 W42711 W65713 AW036375 W4777
W02268 AW135353 AW07785 AW0691 W22240 AW026020 AW153182 AW153984 AW337961 AW373139 AW121122 AW121122 AW121122
AW21234 AW21234 AW0406 AW02033 W62172 AW14066 AW481537 AA329012 AW062409 AW058939 AW25116 W150352 W58206
AW007796 AW88754 AW09675 W0291548 AW135265
W037858 AW088417 BE168022 BE291731 AW05125 AW020393 AW055680 AW439455 AW351821 AW192558 AW062012 AW050210 W199
W63857 AW27874 AW28276 BE16807 AW062328 AW150849 AW20221 W15598 AW161281 AA143491 AW137673 W06001 AW190131 AW148010
W1158232 AW11206 AW192755 AW151911 AW6178 AW43025 AW070927 AW050524 AW078191 AW050524 W435122 AA07834 AW160270
AW093098 W08883 AA340455 AA30631 D08000 AW1153930 AA306488 AA306488 AA306488 AA306488 AA306488 AA306488 AA306488 AA306488
AW202382 AW361185 AW049042 AW355373 AW102688 AW103040 AW352511 AA251810 BE362668 W05452 AA367255 W04712 AW362160
W03039 AW06027 AW05041 AW114128 AW259516 AA315585 AW19051928 AW062735 AW183692 AW1567485 AA05994 AW494149 AW22825
AW032999 AW032999 AW032999 AW032999 AW032999 AW032999 AW032999 AW032999 AW032999 AW032999 AW032999 AW032999 AW032999
W035549 AW14633 W07542 AW032999 AW032999 W11346 AW156986 AW140249 AW033966 AW053453 BE150057 AW037688 AW05059
AW080701 AW065430 AA548989 BE262115 AW157009 AW04590 AW04590 AW04590 AW04590 AW04590 AW04590 AW04590 AW04590
W10308 NML_005107 AW071147 W1031441 W85424 AW140420 AW218572 BE092468 BE030881 AW03877 AW49919 AW394505 W18713
W081283 AW07400 AW054327 BE002229 AW140024 AW147482 AW193337 AW375195 AW22444 AW1900326 AW135033 AW34041 AW176534

WO 02/098358

PCT/US02/17594

N948838 NV235336 NV917287 AD06288 BE040638 AT034240 W19689 A980629 A206433 AA53378 A1406292 AA468838 AD06698
 AD126433 W70601 BE06287 AA533803 AT143147 AD06475 A1496274 A125823 AA039931 A605131 A125823 AA039931 A605131 A125823
 A37434 A3407706 BE06287 AT06467 A030036 A212521 A0674314 A0078805 A533732 A166896 A119680 AD067455 A127468
 AT076944 A1916815 H17814 A4310903 A0013764 A12979 A2402682 AA306035 A0W33399 A0W33399 A353422 AA033427 A0W33395
 5 AD07764 AT036247 AA32601 AD06369 F04621 A224473 A306321 H03904 A483612 AD391543 A0402915 A0402915 A17362 A040291
 A0403113 R04338 A251263 H18346 AD06820 AA03691 T2905 A0951071 L27277 L4778 A075819 B12774 A075819 A12774 A075819
 A068223 BE06287 H03333 N10707 AA03684 A337655 A0W09813 N0337 AA03615 A65347 A0W33399 A0W33399 A353422 AA033427
 A0W33395 A0W33395 A128799 A003219 A044776 A0W43731 A087722 A2445224 AA44751 A412386 N02534 A35491 A009087
 AD236763 A423583 A2296910 A047124 A4236734 A0W514610 H03467 A062607 A046783 A412729 A013495 A068762 A0587374
 A0363731 A427063 A0859757 A221678 A201815 A427063 A230602 A023224 W1988 A058782 A4230918 A0409450 A4227220
 A0765294 A115007 A4230918 A4230918 A4230918 A4230918 A4230918 A4230918 A4230918 A4230918 A4230918 A4230918 A4230918
 A0W46615 AAT31314 A040656 A045431 A0W51901 A0W03676 A0W29470 A0020626 A333034 A350330 A427175 H05978 D20305
 D29155 A021790 BE150364 F01675 A457474 A0466316 A550996 A603780
 100732 14471_11 A057660 W29291 N06862 A000053 BE16801 BE16844 A125823 BE17032 A0W559142 BE168778 BE168778 A431276 AT110136
 A050536 A0516476 A072607 A046265 A487704 W03177 A2096466 W03044 A069362 A527730 A0226683 A0406353 BE16823
 BE15556 W45531 W14322 A000038 A068478 F07078 F01516 N04222 A450708 A0612142 A035558 A035558 A035558 A035558
 A555722 A0505202 H05026 A053344 A0168754 A001162 A140336 W01221 F11347 R2160 H48230 W03324 A111966 A4355731 A0467481
 A1042027 A0W494667 A4545748 A067426 A332120 A663186 H04362 H05083 D55345 N05086 T01202 A020696 D52626 A344264
 D53433 R05265 A085293 A347391 A413006 A044581 A4375416 C04598 A0W23018 A751674 A344636 A344636 A344636 A344636
 A434969 A4351959 A432082 A432082 A432082 A432082 A434148 A434785 A434148 A434785 A434148 A434785 A434148 A434785
 20 A035344 A34356 W07534 A073152 A14248 NML W0190 W0190 W0190 W0190 W0190 W0190 W0190 W0190 W0190 W0190 W0190 W0190
 H24395 A0W175272 A064201 R63636 A066141 A225474 A4465154 A4100348 T54141 A3422661 A442455 H24324 T6832 A342576
 A446779 A51152579 F00575 A058475 A0373220 A063890 A216598 R14889 A114927 A0W32821 H24549 H2384 A443356 A0517496
 R05631 H51274 A058076 H0320 A035227 A046320 R74254 A08065 A06281 A107036 A03305 N07110 A47398 A03305
 A07544 A37151 A008265 A371126 A026299 N0002 A0W0870 A431668 A431668 A431668 A431668 A431668 A431668 A431668 A431668
 25 A035344 A244107 A423940 A354525 A0W19317 A067238 A069285 A4776055 T50374 N62996 N11200 A4262990 A57579
 A528233 A003888 R27013 W08196 W01129 A062740 A0088113 A154627 A147036 R06517 A1305558 A117283 A007126 A068015
 A09337 F2391 F2759 A337879 A552893 A0072388 A4483078 A0W30479 C2134 D46457 A0W15250 A068018 A078127 A068682
 R272174 A0W72402 A058451 A058397 A14326 A051506 A051506 A051506 A051506 A051506 A051506 A051506 A051506 A051506
 A051506 A151506 A051506 A051506 A051506 A051506 A051506 A051506 A051506 A051506 A051506 A051506 A051506 A051506
 W27845 A0W17369 A0582994 A446300 A020000 A001281 A0636202 A0W17222 A0387821 A44630 A472200 A060574 A0514960
 A032654 A0519052 A4573520 A068148 A364847 A0262521 A021640 A0W40299 A51474236 A1919075 A0407287 A4532570
 BE222326 A446657 A057255 N6171 A0515423 A0W47105 A0404746 A40414 A40569354 A02058264 A401138 A0222610
 A061246 A062623 A75193 A071228 A068475 A068475 A072091 A051645 A074647 A074647 A074647 A074647 A074647 A074647 A074647
 A074647 A020912 A0581082 A421268 A0W34206 F03300 A423346 A0W73399 A014885 A0W24024 A122270 A468926 A4242644
 D58122 A0W151942 A059440 A073642 A0572764 A143318 W15228 A1570742 A031278 A0W12098 A3418795 A03418795 A431107
 D57111 A0719308 A4581827 A05236 A001066 D06806 A751498 A082578 A0W82379 A75373 A75373 A75373 D58233 D04743 D07435
 D07135 D57411 N44441 A754630 A0518407 R4509 A0W0806 A0518407 A0518407 A0518407 A0518407 A0518407 A0518407 A0518407
 A000001 D58704 A051815 D58152 D58152 D58152 D58152 D58152 D58152 D58152 D58152 D58152 D58152 D58152 D58152 D58152
 A034400 N65278 A0496915 N65699 A060503 A0W148825 R7735 A033958 W04304 A419311 N26783 A135850 A1376910 A273303
 D107122 A2170472 D57529 H4334 D56712 H11506 A136225 D66661 D66812 N67489 H83245 H03281 A05181935 A044680 D58682
 D524572 H7061 D6867 D6801 D5714 D6328 D6862 D6684 A050516 D68632 D57874 A05181948 D57874 A05181948 D57874 A05181948
 A0264711 A000233 A089915 D57134 D56404 D5940 D57435 D57874 A062384 A0W164074 D22175 F21107 F1932 D5263 D5805
 A3446326 D525 D57728 D57045 A70465 A453331 A1572372 N70924 R4477 A077360 D56991 R12436 R3322 A126163 A429910
 R1692 A0W22331 H03915 Z18795 A051904 F04893 A068387 A068387 A0709116 N7420 A571697 A1446305 A120505 A559264
 A069365 A331 A06745 A07091 T2266 A0W60023 F13791 A459935 A1446305 A4593492
 101386 16685_1 BE26755 A077164 D29458 H1304 A0W24738 N35956 A033712 R91038 N44156 H7774 A413006 R0667 W17532 T52041 A321168
 A059376 A432300 N01167 A414337 T13274 A105194 A074291 C1791 A4351469 A4223315 A0654 A431362 A431362 A036946
 A449334 A551332 A307417 A0639075 A0W67156 F05858 A352838 A353195 A431227 A353195 A431227 A353195 A431227 A353195
 A000001 N46784 A4305477 A460284 N0203 A2062120 D6396156 D6394881 A062786 A361675 H10300 A4146941 A4352975 A404718
 W172771 A419556 A750319 A0W173203 T17633 W03033 W0306 D63969 A030587 A0W46575 A443397 H02819 A1433206 A1433206
 D71061 W00326 A0W0025 A0W0080 A0W30016 A125272 D530333 A042167 A0454395 A419126 A1257854 A420676 W3262
 A068244 W07062 A02048 A052766 A0W129714 A4458794 A455783 A453374 A4716242 A0W03637 W05704 A0W3688 A0W13026
 A0W1904 A4793910 A073887 A0063712 A120343 A4779705 A378985 A048294 A150485 A31445 A369205 A437392 A235022
 A0090502 A47173754 A458766 A47173754 A458766 A47173754 A458766 A47173754 A458766 A47173754 A458766 A47173754 A458766
 A415164 A072761 A071460 A072761 A071460 A072761 A071460 A072761 A071460 A072761 A071460 A072761 A071460 A072761
 A090436 A472062 A012050 A063263 A3035794 A0W37063 A0W70767 A4511332 A353584 A793191 A473893 A114568 A119650
 A061262 A4616632 A336991 A0680475 A0811367 A631256 A424204 A371055 A0715444 A345998 A087834 W37385 A345798
 A0W47778 A142455 A0625718 BE083991 A706402 H06572 A067483 A075441 A024081 A089806 A242706 N2131 A25384 A196444
 D52695 H0681 A057590 N33299 W07066 W06738 A27237 F1591 H7264 A0W02227 A060238 W14744 A410861 A410861 A410861
 A243742 A705312 A0W0230 A068425 A70661 A70661 A70661 A70661 A70661 A70661 A70661 A70661 A70661 A70661 A70661 A70661
 H78941 A0583219 A0W40710 A0583221 A4156119 A0W362077 W04805 A352730 A0W6784 A0W5975 N02638 W7806 A53293
 A0W33708 A0466672 A07294 F04249 A0W455765 A0455765 A42564 H63547 H5040 C03976 H0376 A045252 T4596 R0586 A04691
 D1723 A42591 A0W4263 A0W4263 A072631 BE07671 A103446 A1199916 W17238 A42534300 W0140 A42526 A42526 A42526 A42526
 100220 139161_1 W09091 H4802 A058323 A042768 A428209 A041514 A66880 W1745 F0169 A029152
 116448 30623_1 A0W68161 A419026 A4706022 A4775159 A1738725 A5125234 A4132242 A4312243 A4373154 A4373154 A4373154
 BE26321 BE27064 BE26600 BE10641 A0W47710 A160131 BE30473 BE55970 BE389420 A027965 BE27016 BE50369 BE513878
 BE26394 BE27001 BE136746 A4307170 BE26390 A0W40429 A356963 A0W40632 BE47495 A0W3508 BE468126 A136126 A0710613
 A352826 A41006 N0684 A06836 A154547 A055266 A54956 A470061 A4206105 A53329 A4715272 A0W07890 A067247
 A24840 A469106 A052530 BE04862 A067299 A0W0874 A003231 A0W14026 A4291321 A0W14026 A4291321 A0W14026 A4291321
 A51761 A053212 A052326 A021043 A0W59175 A1282831 A363912 A4151932 A472149 BE271102 BE50816
 A0W72512 A0W23675 NML C03664 F055993 A0627678 A370406 A062241 A1138822 A340524 A0W14026 A4291321 A0W14026 A4291321
 BE44507 A056898 A4742636 A0W06527 A42657 A42657 A42657 A42657 A42657 A42657 A42657 A42657 A42657 A42657 A42657 A42657
 A050178 A4219675 A051905 A050300 A419165 A0W4464 A0W4464 A0W4464 A0W4464 A0W4464 A0W4464 A0W4464 A0W4464 A0W4464
 A058895 BE461614 A0W0826 A35420 A040665 A272881 A057103 A091075 A091075 A091075 A091075 A091075 A091075 A091075 A091075
 A0W117602 A051038 A0770015 A147431 BE222987 A036361 A067116 A067116 A067116 A067116 A067116 A067116 A067116 A067116
 D57822 A053345 A359595 A537304 A4126983 F05994 A026640 N66214 A459493 D20481 H07549 A06841
 A459494 NML A074263 A459494 A459494 A459494 A459494 A459494 A459494 A459494 A459494 A459494 A459494 A459494 A459494
 A459494 A459494 A459494 A459494 A459494 A459494 A459494 A459494 A459494 A459494 A459494 A459494 A459494 A459494
 106847 10525_1 A1147335 A459494 A412396 A307295 N31942 A0W205960 A269376 A1129067 A0W0195 A0W02474 A36408 A076661 A136820
 106657 23226_7 BE596773 A0484916 A411356

WO 02/098358

PTC/US02/17594

					106658	112832_1	AA461696 AA113139 AA074186 AA063045 AA074392 AA063159 AA113057 AA094307
					115851	26310_1	NM_005758 58 1552 AA337668 W52664 AA438725 AA152634 AA000488 AB512155 AA072456 AA643329 W32478 AA435577 AA00782
							AZ289997 AA782155 AA130762 AA130771 11046809
5		102012	21793_1				BE293035 AUJ77338 U30657 NM_003088 AW732635 AL154784 AL120159 BE409658 T09062 BE297271 BE294908 BE273148 BE295718
							BE295070 BE294930 BE406153 BE287652 BE281074 BE280804 U00973 NM101021 BE294787 BE276923 BE262072 BE263517 BE263517
							BE263507 AA177408 BE296430 AW000297 BE530003 AA000433 BE263544 BE287001 AA1428010 T77482 BE263508 BE39341
							AA077541 W67538 AW005065 AA096869 T49230 BE272643 BE268670 BE279826 AW040330 A9436035 BE019144 BE269451 AA77265
							BE272651 BE081948 BE269795 BE390014 AA852153 BE312227 BE262009 W070505 AA043192 AA403111 AL134704 AA459745 AA027019
10							W07875 BE265292 AW166944 AA461918 AL116868 A1167100 W086333 AA339482 AA000054 AA337668 AA337668 AA337668 AA337668
							BE208565 AU07647 W00643 A337668 BE207898 W00489 AA000433 AA000282 AA000511 AA000282 AA000511 AA000282 AA000511
							BE300543 AA552221 AA000311 BE312463 AA551111 AB081665 W11338 A3777719 AL1141565 BE420354 A5327709 AA502125 A530276
							BE206871 AL475936 BE493627 A2001615 NM467734 AA300886 AW297260 AW363002 AW153534 BE207810 AA481327 W68528 AU01541
							AW126375 AL167956 AA167956 AA726177 W026859 W51199 W02020 A395697 AW360528 AW362220 A501854 A453087 A3822508
15							AA149454 AA177107 AA152557 W02719 B52745 AA440100 W00814 AA152733 A215944 AB57035 A300922 A50780 A50780 A50780
							AZ28904 AA000308 AA607127 AW10593 AA175346 AA015531 A3307297 AA024564 AB68845 AB671213 AA556489 AB50618 AA1001577
							AZ333981 A558453 A556375 W594745 A5141983 AW196606 A556903 A3006227 A087087 AA393660 A056505 A556126 A010122
							AW140122 AA527004 A814950 AW047073 A5566075 AW073874 AW190325 AA555476 AB654701 A354353 AA456248 AW150618 A354918
							AW10359 A500094 T08432 AW004384 AW005167 AB027238 AW126669 AW027110 W095735 AA515596 I42219 W47264 W61253 A380715
20							AA559515 BE151908 AA03988 A509143 AA527613 A502542 AA43405 A501070 A341011 BE169185 A502897 A502897 A502897
							AA533512 AA09044 AA033670 AA033222 AA063975 AA035555 A5170146 A5121100 W02739 W02155 AA071406 AA52295 A146561
							AA338493 AA045494 BE211997 BE268624 BE311788 BE269836 BE313211
25	132116	96515_1					AW060474 AA320243 AA04789 A086169 N20591 AB234476 H81760 AA406184 W41975 A040099 A4033348 AA323234 BE269273
							AA114345 AA064294 AA394165 AA194516 BE269595 A565992 AZ297091 A4041881 A3494477 W00276 A2342457
							W7792 A0052193
30	102034	598_1					A930474 A190475 W27913 AL103029 A903264 A903363 A903473 A903426 A903263 A903331 A903364 AA45814 AA45814 W75456
							NM_000232 AA016495 AA68437 AA336463 AA336866 U06291 AA339073 A360007 I26476 AL151040 A45110 H0222 AA411110
							BE184970 R08082 H14437 BE184986 BE184957 BE184972 BE184961 BE184984 BE184930 AA23819 A4858471 H14444 H4437 L24 H2970
							H02523 H55914 AA09045 BE184936 AA336770 BE184958 BE184961 BE184951 H02626 T2790 BE184900 AA09049 BE184965 BE3647
							W55326 T49159 A134472 AA149444 BE195907 A500740 AW151000 A440405 AA581715 A674698 A532373 A5471387 AA411130
							AA174604 H02623 AW339955 AA008830 A143336 A805155 AW0073726 A51079149 A806149 A855131 A132299 AB07197 A82374 H24200
							A525436 AA193948 AL16049 A342425 A981284 A591548 A530927 A240267 A015587 A5433989 AA427366 A112768 A10348 A10348
							A911417 AA42626 A340733 AL104682 AA44364 A421359 A129080 A869379 W513294 H25317 AA094143 H20268
							T489744 A347112 BE184765 H48477 AA671098 W48391 AA461539 A487962 A133891 AB5777 A532747 A203022 W61710 A298200
35							AW145725 H25216 A1401719 AA4249621 A0191917 A4663157 A5N1306 A627876 W61309 W48716 AA468748 T48914 A116001
							R08083 A091062 AB04537 R51837 A127238 AA424955 AA424948 A558237 AB5774 A194396 A1271628 A442125 A147369 A481104 H0032
							A2114418 AW002315 A512675 A393603 AA052904 A558237 AB5774 A194396 A1271628 A442125 A147369 A481104 H0032
							AW126236 AW27507 AW06966 A62771 AW263315 AW160184 AA22100 H21232 AW15114 A24515 AA26579 A58179 A33966
							AW16539 AW003451 BE062208 AW593940 W5734 AHT3435 A501983
40	102076	28041_1					BE29979 Z35966 AA247234 AW249122 U06579 AW124566 AW250360 AA250483 BE241687 BE249400 A27005 A270237 AA380810
							BE26876 AW003908 BE081835 AA151660 AA053842 BE269683 BE267145 L2165 L2610 U03081 B87388 AA27775 AA46465 W01311
							BE163645 BE267095 AW33606 BE263622 BE263601 BE297240 AA333230 BE263608 BE263608 BE263608 BE263608 BE263608
							L47238 BE207178 T09388 BE263622 A54282 BE263678 BE263621 AA139190 A556605 BE263672 A240219 AA460448 AA00447
							AW543745 AA378396 A5321991 A310434 AA294192 R64671 A084373 AA378396 D31116 AA378719 AA095029 A532199 AA378396
							AW145725 W02624 H83378 W73002 R74301 BE454783 BE266095 R57900 BE159826 A375519 A537832 T8331 W39472 W44413
							A080210 R79427 AW246238 H44812 AA378207 R27374 BE265653 BE267082 A373608 AW074396 A1874394 A378207 A502690 A145492 B58402
							AA373408 AW167163 A5320918 AA178563 AA254249 AA178216 T13540 AW246587 A005010 A441072 A026800 A145492 B58402
							AA39747 AW09004 AW090491 W74365 AW090497 AA481474 AA183394 AA5401012 A457424 AA484559 AW19698 A382905 AA1451214
							W420428 N2341 A775303 N36012 A098480 W6550 N35823 R27375 A1238939 N3064 A559065 A146429 A818625 N33402 C25587
50							AA176735 A3495 N35248 C2315 AW099033 A302439 A4134583 A494413 BE004794 A919187 A0119593 A455459 A401908 A089191
							A432626 APT11930 A431697 A402728 A752794 A507619 A090396 A751689 A54518 A570573 R47673 W4535 AW192512
							AA670001 AA000308 A355986 AB06220 AW115372 W44546 A500724 A500724 A500724 A500724 A500724 A500724 A500724
							AW163718 BE301970 AWT12949 AW001384 AWT732066 R79426 A540886 AB14746 A671072 A13334543 A157653 A95572 AWT25045
							BE046057 BE032155 A622388 A066427 A0669702 T754512 A274183 A818343 AA36866 A818343 A818343 A818343 A818343
55							AW176511 A867247 AA451363 A815963 A815963 A815963 A815963 A815963 A815963 A815963 A815963 A815963 A815963
							BE176511 A815963 A815963 A815963 A815963 A815963 A815963 A815963 A815963 A815963 A815963 A815963 A815963
							A500446 W44648 AW591391 A0023831 T29732 A505216 A066902 T33382 R87514 A1147453 A497241 AW083649 A91521 BE27943
							W00887 A001936 AB08847 AB872642 A270635 A6226537 A60140 A601560 AWT5689 AWT5689 AWT5689 AWT5689 AWT5689
							W00887 A232834 A674560 A672555 A509141 A5454813 A5051591 A277441 A514373 A47345 A484419 A4096999
							AW26955 F32303 AHT537 A080594 A51514 A688374 A68543 A427034 A529255 A529255 A529255 A529255 A529255
							AA17854 A770593 A197453 A197444 A406967 A671545 A531916 A437702 A027095 A441004 A77144 A584363 A200239
							BE267310 AA374790 W00896 AA112103 BE267320 AA52676 N42717 W24033 N35290 BE261686 BE26688 AW592075 R32687 AWT46894
							W40328 T25822 A0229873 BE26034
							W26436 AW135972 BE349103 A505418 R54810 AB04004 A079147 A912294 A339626 N40443 A873997 AA148820 AA4118512
							AA10521 A281770 A272964 A505699 A505699 A505699 A505699 A505699 A505699 A505699 A505699 A505699
65	132160	128656_1					A822529 AW248872 H09511 AWT779657 AB92254 A030377 A5152171 A5152171 A5152171 A5152171 A5152171 A5152171
							AA05612 AA045480 A27343 A513008 AWT139975 A635838 A5054603 AW000790 A208239 A275835 AW090294 A4021587 AWT73455
							H095126 W2649424 A40222 A002572 BE2606145 A1129688 BE3630456 A0129997 A2A9409 A840368 A4470364 A2411794
							AW126655 F32303 AHT537 A080594 A51514 A688374 A68543 A427034 A529255 A529255 A529255 A529255 A529255
							AA17854 A770593 A197453 A197444 A406967 A671545 A531916 A437702 A027095 A441004 A77144 A584363 A200239
							BE267310 AA374790 W00896 AA112103 BE267320 AA52676 N42717 W24033 N35290 BE261686 BE26688 AW592075 R32687 AWT46894
							W40328 T25822 A0229873 BE26034
							W26436 AW135972 BE349103 A505418 R54810 AB04004 A079147 A912294 A339626 N40443 A873997 AA148820 AA4118512
							AA10521 A281770 A272964 A505699 A505699 A505699 A505699 A505699 A505699 A505699 A505699 A505699
70	132164	10290_1					AA05612 AA045480 A27343 A513008 AWT139975 A635838 A5054603 AW000790 A208239 A275835 AW090294 A4021587 AWT73455
							H095126 W2649424 A40222 A002572 BE2606145 A1129688 BE3630456 A0129997 A2A9409 A840368 A4470364 A2411794
							AW126655 F32303 AHT537 A080594 A51514 A688374 A68543 A427034 A529255 A529255 A529255 A529255 A529255
							AA17854 A770593 A197453 A197444 A406967 A671545 A531916 A437702 A027095 A441004 A77144 A584363 A200239
							BE267310 AA374790 W00896 AA112103 BE267320 AA52676 N42717 W24033 N35290 BE261686 BE26688 AW592075 R32687 AWT46894
							W40328 T25822 A0229873 BE26034
							W26436 AW135972 BE349103 A505418 R54810 AB04004 A079147 A912294 A339626 N40443 A873997 AA148820 AA4118512
							AA10521 A281770 A272964 A505699 A505699 A505699 A505699 A505699 A505699 A505699 A505699 A505699
							AA05612 AA045480 A27343 A513008 AWT139975 A635838 A5054603 AW000790 A208239 A275835 AW090294 A4021587 AWT73455
							H095126 W2649424 A40222 A002572 BE2606145 A1129688 BE3630456 A0129997 A2A9409 A840368 A4470364 A2411794
							AW126655 F32303 AHT537 A080594 A51514 A688374 A68543 A427034 A529255 A529255 A529255 A529255 A529255
							AA17854 A770593 A197453 A197444 A406967 A671545 A531916 A437702 A027095 A441004 A77144 A584363 A200239
							BE267310 AA374790 W00896 AA112103 BE267320 AA52676 N42717 W24033 N35290 BE261686 BE26688 AW592075 R32687 AWT46894
							W40328 T25822 A0229873 BE26034
							W26436 AW135972 BE349103 A505418 R54810 AB04004 A079147 A912294 A339626 N40443 A873997 AA148820 AA4118512
							AA10521 A281770 A272964 A505699 A505699 A505699 A505699 A505699 A505699 A505699 A505699 A505699
							AA05612 AA045480 A27343 A513008 AWT139975 A635838 A5054603 AW000790 A208239 A275835 AW090294 A4021587 AWT73455
							H095126 W2649424 A40222 A002572 BE2606145 A1129688 BE3630456 A0129997 A2A9409 A840368 A4470364 A2411794
							AW126655 F32303 AHT537 A080594 A51514 A688374 A68543 A427034 A529255 A529255 A529255 A529255 A529255
							AA17854 A770593 A197453 A197444 A406967 A671545 A531916 A437702 A027095 A441004 A77144 A584363 A200239
							BE267310 AA374790 W00896 AA112103 BE267320 AA52676 N42717 W24033 N35290 BE261686 BE26688 AW592075 R32687 AWT46894
							W40328 T25822 A0229873 BE26034
							W26436 AW135972 BE349103 A505418 R54810 AB04004 A079147 A912294 A339626 N40443 A873997 AA148820 AA4118512
							AA10521 A281770 A272964 A505699 A505699 A505699 A505699 A505699 A505699 A505699 A505699 A505699
							AA05612 AA045480 A27343 A513008 AWT139975 A635838 A5054603 AW000790 A208239 A275835 AW090294 A4021587 AWT73455
							H095126 W2649

WO 02/098358

PTC/2002/17594

AW328148 AA309056 A33534144 AA341060 TB9004 T28074 T47716 AA129944 AA062195 A1935574 T93111 H56577 N91 324 AA002115
BE774418 BE58118
AA55324 AA244003 NML 001099 M97589 JS3005 T29624 M24902 XS2174 M34540 U07097 AA24034 AA37422 AA371462 A1551752
AA371312 AA550056 AA370116 AA370957 AA370806 AA565052 AA642055 AA405335 AA492280 AA669716 AA527805 AA530327 AA398977
AA224875 AA228288 AA115631 AA47435 AA370186 AA400267 AA564494 AA221771 AA002979 AA507771 AA681674 AB21867 AA220721
AA68138 AA226366 AA613930 AA225411 AA67236 AA505831 AA573645 AA684967 AA003374 AA279653 AA458334 AA51198 AA504327
AA654078 AA324778 AA450281 AA370186 AA304845 AA647818 AA441709 AA530837 AA492280 AA527805 AA530327 AA398977
AA565652 AA815512 AA82518 AA503300 AA659545 AA974889 AA563365 AA633663 AA492232 AA236653 AA91551 AA810547 AA970897
AA333338 AA379205 AA641165 AA574271 AA224875 AA602106 AA605053 AA613200 AA635465 AA41194 AA574278 AA359820 AA219380
AA57806 AA451731 AA640677 AA252529 AA225232 AA537057 AA507771 AA51819 AA645008 AA278451 AA220672 AA503139 AA665355
AA512824 AA515715 AA450616 AA519791 AA473630 AA500710 AA458100 AA407045 AA662687 AA559131 AA523583 AA680671 AA251646
AA275398 AA404552 AA502272 AA393911 AA226687 AA540364 AA417799 AA543288 AA637931 AA370592 AA451077 AA422522 AA640331
AA643799 AA387215 AA603653 AA545498 WS7824 AA468243 AA033506 AA225449 AA657510 AA459483 AA507890 AA468574 AA727171
AA92165 AA503918 AA502090 AA224545 AA309621 AA579441 AA468201 AA531368 AA320147 AA600430 AA482137 AA821137 AA547755
AA922979 AA467730 AA732062 AA493260 AA664424 AA226678 AA656439 AA574147 AA465851 AA225783 AA533875 AA225511 AA467730
AA273205 AA406300 AA225680 AA427619 AA225698 AA971653 AA502080 AA658392 AA661393 AA459972 AA225783 AA533875 AA225511
AA225365 AA507972 AA507213 AA589173 AA526555 AA810657 AA128633 AA970693 AA971003 AA978305 AA532626 AA225414 AA532179
AA636047 AA656361 AA679597 AA527905 AA228755 AA225135 AA230012 AA507232 AA573801 AA947979 AA492253 AA468574 AA494247
AA662578 AA449233 AA506231 AA589713 AA580004 AA680039 AA513784 WS7582 AA468080 AA355753 AA531127
AA304770 WS5035 AA450616 AA942811 T23259 T66714 AA671513 L137374 BE12661 BE1175 BE207100 BE203320 BE08115
AA573900 BE354830 AA047547 AA775952 BE378702 AA468713 L110111 T03540 AA006991 BE547280 AA355703 AA581520 AA573331
AA589720 AA587206 AA6275873 BE408229 AA9188148 BE255166 BE257511 AA9753727 AA373141 AA581518 AA811223 AA306960
AA230283 AA952080 BE257409 AA003502 AA005085 C00012 BE312741 BE407213 AA209362 AA298199 AA258553 AA914787 AA731722
BE205085 AA719872 AA915446 BE301699 AA915520 AA485174 AA460257 AA1196518 AA564533 AA112879 AA9719252 AA971485
AA604650 AA32744 AA782447 AA60294 AA125548 AA832324 AA811125 AA258553 AA914787 AA460257 AA485174 AA731722
AA892025 AA36341 AA097597 AA928513 AA358774 BE243487 AA462053 AA632937 AA252690 T10110 T03540 AA40854 AA403844 AA403800 AA16438
WS3328 T2884 AA857010 AA854661 BE12575 BE388740 T56780 AA371338 BE28871 AA489971
T05150 T12741 WS0503 WS0524 M26674 AC004080 AA61296 AA595382 AA224113 AA548822 AA811687 AA0032129 AA504935
AA223317 AA972578 AA955416 AA370186 AA910417 AA917935 AA441298 AA478898 AA21895 AA507890 AA468574 AA727171 BE263900
AA118482 AA605654 AA705301 N87578 WS4705 WS4340 AA623789 N80725 AA1081840 T23089 AA951105 AA951089
AA009684 AA758732
U14134 AA083438 AA665238 T84788 A515178 AA285856 AA975896 AA065334 AA753263 AA023078 AA281569
X80321
AA103027 AA550628 AA525154 AA749606 T14835 A574402 AA66441 AA306911 AA769992 AA95656 A735376 WS29609 AA9733977
AA970289 AA140433 BE485241 T51261 AA507168 BE536600 AA151548 AA17003 AA750203 AA159991 AA36488 AA143718 AA40080
BE155600 AA002929 N33271 T118989 A971008 A57065 AA33233 BE550457 A978784 AA335026 AA105077 AA0503 AA3549570 AA970289 AA973682
N33731 A1379046 AA47314 AA77833 BE60821 AA2179821 AA186884 BE46987 AA011810 BE360896 A141848 AA540729 R86085 R02046
BE7803 AA118524 NPT54 AA926551 AA347405 AA114154 AA98744 AA11540 BE97343 AA118524 AA926551 AA970289 AA973682
N913671 BE221332 BE465957 AA428088 AA1254 BE225793 AA213458 AA941526 AA24001 AA526729 AA972638 AA95105 AA575044
AA50486 AA531009 AA800711 AA928798 F56561 AA852667 AE752234 A750727 H53306 AE765216 AA701531 AA852160 A821997 AA70861
T53485 AA506539 AA85345149 T30031 AA021969 AA750937 AA350669 T53494 AE753507 AA971995 AA812632 AE78928 AA26336 AE719435
BE7656 AA928158 AA023108 R80032 X142334 AA714605 R80930 AA413334 AA030939
D21282 AA119130 AA130824 M05417 AA797190 AA33206 AA451697 AA355729 AA36073 AA36073 AA36073 AA36073 AA36073
A913175 AA81058 AA947975 AA825228 BE259115 AA958157 AA979319 AA854695 BE167356 AA08910 AA307111 AA08910 AA08910
A0242662 AA001637 A540378 AA83431 AA846164 AA854610 AA14585 AA8500478 AA83435 AE018761 AA907075 AA84206 AA2437821
A023365 BE21592 AA317945 AA87463 AA83434 AA918607 AA4001112 AA382499 AA765881 AA365577 BE260473 BE464372 AA37020
AA904317 AA919415 AA191216 AA141997 AA986673 AA347506 AA973507 AE73362 AE719116 AA112112 AA80433 F08714 AA730377
AA292811 AA24182 AA307171 N08310 AA951669 H07013 AA813959 AA913704 R14033 AA604903 F08513 H7599 BE457899 BE3670
A712189 A347405 AA716645 AE719450 AA586782 AA906550 AA512144 W0312 T10258 AA830283 DE069171 AA952001 AA95189 BE3970
AA918996 AA952000 AA479364 AA488526 T97118 AA370129 AA128268 AA04505 AA040445 AA251278 R09597 R07421 AA133589
H05073 AE290355 AA465246 BE765365 AA4237043 AA552705 WS7556 H2420 D15586 WS664 AA251321 H77196 AA061505
AA966335 BE03247 W01508 BE36064 AA740768 Z14772 H22678 AA4226 HA6705 WS7378 AA740951 AA617204 AA128701 H56303
W53571 AA025405 AA237649 AA271261 AA869834 BE463099 T49492 AA194804 AA81613 AA165844 BE592392 A222920 H0474 AA18978
HA461421 AA818338 AA195465 BE467847 AA650524 T68392 AA002213 BE047333 AA96134 HA46726 AA87878 AA35821 AA98789
AA978365 AA20228 AA950502 H04212 H73355 AA827684 H05462 HA6184 AA898708 AA004273 H73026 AA098827 AA737525 A227946
AA302533 AA511481 AA950582 BE0327 H609221 BE040732 AA08149 AA41395 BE26940 AA814101 AA130791 AA31272 AA35196
AA787715 AA569154 AA911816 L125439 AA623024 AA2135930 AA5387307 AA51556 A8522728 WS6526 AA22010 W06795 AA91587
AA294272 HA6032 AA091106 AA161324 AA63814 AA825415 A8522055 AA335610 AA93498 R16744 AA575537 H10783 N0708 BE2578
AA576105 WS2682 D23057 AA091148 AA18992 AA1142728 AA659067 AA826189 AA465138 AA1122598 T29720 AA4732157 AA83939 Z14774
H51425 AA644679 AA836329 AA70808 F8470 AE74000 AA48714 AA140246 AA825356 BE712272 F04843 AA43371 AA435196
H55141 AA82586 AA243635 AA219415 AA937807 T87440 AA271627 T14549 AA02148 AA61588 AA44711 AA96932 AA4113958 AA503365
AA35880 AA243243 AA215941 AA773821 R06175 AA034227 HA6108 HA6163 HA6279 HA6604 H62521 T97033 AA514807 AA906635
AA960750 AA906755 AA906640 BE301924 BE324562 AA124093 A020635
AA25888 AA300021 AA970688 AA9917357 AA715623 AA715780 AA715789 AA978267 AA916258 N2762 AA915986 AE138629
AA345633 T94453 N95435 AA138586 AA107065 AA9855 AA9855 AA9855 AA17844 AE74345 AA92368 N91780 AA4005 AA52501 W59159
BE138384 AA341708 AA146038 BE565222 W36579 W7170 AA229471 AA37304 AA434321 W29955 W69286 AA010132 W6226 AA45361
W05009 AA31998 F2522 AA150856 W0368 AA040467 AA046161 Z3 N03590 AA035042 AA385776 AA188329 H5383 AA906336 AA577569
H72429 F25637 AA000233 H23866 DE2811 AA352610 AA413578 BE379946 AA973909 AA434375 AA916145 AA439265 W94755 F4408
W15245 AA55053 AA09400 BE38297 AA55053 AA02040 AA24819 AA18324 AA624437 AA364860 AA9394 AA9394 AA9394
N09903 F1088 BE36430 W43291 AA149322 AA13324 AA14653 AA634771 W81977 AA41588 AA44101 AA694378 AA107890 F34059
W15392 AA812656 AA89736 F27755 AA576121 AA143774 AA716386 AA470096 AA919120 F2381 AA106086 AA36216 AA0071769
AA278832 F35653 AA88861 A493729 AA709640 AA193686 AA687825 A191996 AA74545 AA695949 AA716240 AA9157928 AA892260
AA748006 AA107874 AA645458 AA514577 AA226212 AA722829 AA970192 AA37121 AA914369 AA296703 W7987 AA229462 AA773398
AA344333 AA014149 AA126657 AA933279 F3006 F30063 AA126661 AA126661 AA126661 AA126661 AA126661 AA126661 AA126661 AA126661
A12653 AA126661 AA144014 AA126661 AA27654 AA00738 AA00738 AA00738 AA00738 AA00738 AA00738 AA00738 AA00738
AA040332 AA701751 F30312 AA263653 AA002924 AA742842 AA72838 F20313 AA70661 A5811659 AA2584 AA626130 AA46242 AA643339
AA463338 AA725774 AA18758 AA834435 AA941857 F34887 F32905 AA353786 AA719543 AA88600 AA54646 AA88601 BE12993 F24926

PCT/US02/17594

PCT/US02/17594

PCT/US02/17594

1

PCT/US02/17594

1

PCT/US02/17594

1

PCT/US02/17594

1

WO 02/098358

PCT/US02/17594

[illegible]

PCT/US02/17594

PCT/US02/17594

PCT/US02/17594

12

PCT/US02/17594

1

PCT/US02/17594

WO 02/098358

PCT/US02/17594

BE177710 HA3742 AA130321 H05246 AWB17890 AWB11678 AWB198136 AA411576 AWB34870 AWB171726 N99045 AW190050 W48791
 R98148 AW129654 AWB51778 AA123240 AA147092 AWB29905 AWB51914 AW129655 AW147510 AA159593 AW129656 AA1277152
 A1864003 A1869956 AA594584 AW063760 AWB37169 AA11440 220745 A W069342 A65-4272 AW05768 AWB6524 AW190197 AW123438
 AW103196 A050046 A1853626 AW00547 A1858431 AA554141 AW10745 U82771 AA431957 AA622702 AA101026 AA505254 A1413194
 A1770195 BE00476 A133696 D20039 BE001103 BE000729 AW03673 A1129438 AW038158 AW14056 AW120660 A121741 A473470
 AAT81550 AA847245 AW97728 A145918 A725251 AA106867 AW01490 AWB01890 AW01891 A1857605 AW027254 A1869548 AW068510
 A1029255 A206961 A1127564 A186657 A171239 A185741 A103043 A187146 A103043 A187146 A103043 A187146 A103043 A187146
 A0693396 AA935311 A1521264 R55066 W76707 A1272345 AA115005 A413764 A1805056 AW47042 A134375 A105203 A2076704
 W06165 W61209 AW056530 W06348 A465662 A244933 A2331 A5 AWB03165 H06551 A037252 W61292 AW476328 A47764 W6184
 A1767715 A1534509 A4843429 A7101333 A1161902 A242640 A490338 AW119891 A124393 A4537997 AA10742 R06130 A473111
 A1323119 A1245104 A1857106 A64622 158945 AW172595 A1057631 A185258 C7526 AW423040 F02135 A1221319 F0441 AW70496
 F0614 A1056083 A2541277 128647 A1858101 A455668 AW282111 A1147151
 BE262906 BE245866 BE244814 BE230404 A100724 A100727 BE263251 BE131253 BE268006 AA142320 AW03780 A0482209
 A12013209 NM 101237 A151688 A1158802 X53003 AA360411 A1001326 AW046728 A061440 AW67571 A1654232 A0371160 A1004666
 AW171028 A12713393 A10430547 A077210 A1036671 A107436 A184464 A141638 AA48287 A072243 AW126757 A1191011 A1303495
 A1138003 A1016683 A1869661 T23292 AW001086 AW001916 A1213394 A1857629 A187825 BE54910 A1857629 A1857629 A1857629
 R90901 A1020424 R43162 R37467 H00387 AA367338 AW555845
 A1264847 A101 A1851497 A1863821 A1867620 AW06292 A1672346 AW00300 N101071 A6111641 AW16660 A116823 A131201 R3335
 A0001691 R09991 BE20785 AW14257 A102952 AA22354 A1008748 A186741 A186741 A186741 A186741 A186741 A186741 A186741
 W94015 AW51691 A183618 N02349 F03925 F13300 A23564 A183618 A183618 A183618 A183618 A183618 A183618 A183618
 A153554 A153518 A183774 A102025 AW00834 A18675256 AW06300 A088420 A50307 A1867527 A1867527 A1867527 A1867527
 A1865657 A1869986 AA22447 AA54152 AW066040 A070073 A4573096 A057436 A1071118 A093330 A14273819 A1692626 AW127648
 A4522067 AW134300 A00341 A124771 A1478720 BE139653 A1614032 A1241716 AWB14196 A2424116 AA424321 AA424321 AA424321
 A1857679 A1849575 AA506033 AW000765 A1825647 A1867711 A123686 A0037412 A1849576 AW1990633 A1868349 A1869113 A1869113
 A254582
 R44714 A1862896 A623116 A1271632 T10160 Z40966
 D06962 Z43779 AA26247 A070337 A000017 BE396788 BE146000 A140003 A186951300 BE326763 A565133 T11443 AW191729 Z39644
 AW148267 R44776 W4028 AA133831 D81179 AW292596 W42633 A434033 A18674678 R33792 Z2006 A04212946 AW1665565
 W94015 AW51691 A183618 N02349 F03925 F13300 A23564 A183618 A183618 A183618 A183618 A183618 A183618 A183618
 A153554 A153518 A183774 A102025 AW00834 A18675256 AW06300 A088420 A50307 A1867527 A1867527 A1867527 A1867527
 A1865657 A1869986 AA22447 AA54152 AW066040 A070073 A4573096 A057436 A1071118 A093330 A14273819 A1692626 AW127648
 A4522067 AW134300 A00341 A124771 A1478720 BE139653 A1614032 A1241716 AWB14196 A2424116 AA424321 AA424321 AA424321
 A1857679 A1849575 AA506033 AW000765 A1825647 A1867711 A123686 A0037412 A1849576 AW1990633 A1868349 A1869113 A1869113
 A254582
 R44714 A1862896 A623116 A1271632 T10160 Z40966
 D06962 Z43779 AA26247 A070337 A000017 BE396788 BE146000 A140003 A186951300 BE326763 A565133 T11443 AW191729 Z39644
 AW148267 R44776 W4028 AA133831 D81179 AW292596 W42633 A434033 A18674678 R33792 Z2006 A04212946 AW1665565
 W94015 AW51691 A183618 N02349 F03925 F13300 A23564 A183618 A183618 A183618 A183618 A183618 A183618 A183618
 A153554 A153518 A183774 A102025 AW00834 A18675256 AW06300 A088420 A50307 A1867527 A1867527 A1867527 A1867527
 A1865657 A1869986 AA22447 AA54152 AW066040 A070073 A4573096 A057436 A1071118 A093330 A14273819 A1692626 AW127648
 A4522067 AW134300 A00341 A124771 A1478720 BE139653 A1614032 A1241716 AWB14196 A2424116 AA424321 AA424321 AA424321
 A1857679 A1849575 AA506033 AW000765 A1825647 A1867711 A123686 A0037412 A1849576 AW1990633 A1868349 A1869113 A1869113
 A254582
 R44714 A1862896 A623116 A1271632 T10160 Z40966
 D06962 Z43779 AA26247 A070337 A000017 BE396788 BE146000 A140003 A186951300 BE326763 A565133 T11443 AW191729 Z39644
 AW148267 R44776 W4028 AA133831 D81179 AW292596 W42633 A434033 A18674678 R33792 Z2006 A04212946 AW1665565
 W94015 AW51691 A183618 N02349 F03925 F13300 A23564 A183618 A183618 A183618 A183618 A183618 A183618 A183618
 A153554 A153518 A183774 A102025 AW00834 A18675256 AW06300 A088420 A50307 A1867527 A1867527 A1867527 A1867527
 A1865657 A1869986 AA22447 AA54152 AW066040 A070073 A4573096 A057436 A1071118 A093330 A14273819 A1692626 AW127648
 A4522067 AW134300 A00341 A124771 A1478720 BE139653 A1614032 A1241716 AWB14196 A2424116 AA424321 AA424321 AA424321
 A1857679 A1849575 AA506033 AW000765 A1825647 A1867711 A123686 A0037412 A1849576 AW1990633 A1868349 A1869113 A1869113
 A254582
 R44714 A1862896 A623116 A1271632 T10160 Z40966
 D06962 Z43779 AA26247 A070337 A000017 BE396788 BE146000 A140003 A186951300 BE326763 A565133 T11443 AW191729 Z39644
 AW148267 R44776 W4028 AA133831 D81179 AW292596 W42633 A434033 A18674678 R33792 Z2006 A04212946 AW1665565
 W94015 AW51691 A183618 N02349 F03925 F13300 A23564 A183618 A183618 A183618 A183618 A183618 A183618 A183618
 A153554 A153518 A183774 A102025 AW00834 A18675256 AW06300 A088420 A50307 A1867527 A1867527 A1867527 A1867527
 A1865657 A1869986 AA22447 AA54152 AW066040 A070073 A4573096 A057436 A1071118 A093330 A14273819 A1692626 AW127648
 A4522067 AW134300 A00341 A124771 A1478720 BE139653 A1614032 A1241716 AWB14196 A2424116 AA424321 AA424321 AA424321
 A1857679 A1849575 AA506033 AW000765 A1825647 A1867711 A123686 A0037412 A1849576 AW1990633 A1868349 A1869113 A1869113
 A254582
 R44714 A1862896 A623116 A1271632 T10160 Z40966
 D06962 Z43779 AA26247 A070337 A000017 BE396788 BE146000 A140003 A186951300 BE326763 A565133 T11443 AW191729 Z39644
 AW148267 R44776 W4028 AA133831 D81179 AW292596 W42633 A434033 A18674678 R33792 Z2006 A04212946 AW1665565
 W94015 AW51691 A183618 N02349 F03925 F13300 A23564 A183618 A183618 A183618 A183618 A183618 A183618 A183618
 A153554 A153518 A183774 A102025 AW00834 A18675256 AW06300 A088420 A50307 A1867527 A1867527 A1867527 A1867527
 A1865657 A1869986 AA22447 AA54152 AW066040 A070073 A4573096 A057436 A1071118 A093330 A14273819 A1692626 AW127648
 A4522067 AW134300 A00341 A124771 A1478720 BE139653 A1614032 A1241716 AWB14196 A2424116 AA424321 AA424321 AA424321
 A1857679 A1849575 AA506033 AW000765 A1825647 A1867711 A123686 A0037412 A1849576 AW1990633 A1868349 A1869113 A1869113
 A254582
 R44714 A1862896 A623116 A1271632 T10160 Z40966
 D06962 Z43779 AA26247 A070337 A000017 BE396788 BE146000 A140003 A186951300 BE326763 A565133 T11443 AW191729 Z39644
 AW148267 R44776 W4028 AA133831 D81179 AW292596 W42633 A434033 A18674678 R33792 Z2006 A04212946 AW1665565
 W94015 AW51691 A183618 N02349 F03925 F13300 A23564 A183618 A183618 A183618 A183618 A183618 A183618 A183618
 A153554 A153518 A183774 A102025 AW00834 A18675256 AW06300 A088420 A50307 A1867527 A1867527 A1867527 A1867527
 A1865657 A1869986 AA22447 AA54152 AW066040 A070073 A4573096 A057436 A1071118 A093330 A14273819 A1692626 AW127648
 A4522067 AW134300 A00341 A124771 A1478720 BE139653 A1614032 A1241716 AWB14196 A2424116 AA424321 AA424321 AA424321
 A1857679 A1849575 AA506033 AW000765 A1825647 A1867711 A123686 A0037412 A1849576 AW1990633 A1868349 A1869113 A1869113
 A254582
 R44714 A1862896 A623116 A1271632 T10160 Z40966
 D06962 Z43779 AA26247 A070337 A000017 BE396788 BE146000 A140003 A186951300 BE326763 A565133 T11443 AW191729 Z39644
 AW148267 R44776 W4028 AA133831 D81179 AW292596 W42633 A434033 A18674678 R33792 Z2006 A04212946 AW1665565
 W94015 AW51691 A183618 N02349 F03925 F13300 A23564 A183618 A183618 A183618 A183618 A183618 A183618 A183618
 A153554 A153518 A183774 A102025 AW00834 A18675256 AW06300 A088420 A50307 A1867527 A1867527 A1867527 A1867527
 A1865657 A1869986 AA22447 AA54152 AW066040 A070073 A4573096 A057436 A1071118 A093330 A14273819 A1692626 AW127648
 A4522067 AW134300 A00341 A124771 A1478720 BE139653 A1614032 A1241716 AWB14196 A2424116 AA424321 AA424321 AA424321
 A1857679 A1849575 AA506033 AW000765 A1825647 A1867711 A123686 A0037412 A1849576 AW1990633 A1868349 A1869113 A1869113
 A254582
 R44714 A1862896 A623116 A1271632 T10160 Z40966
 D06962 Z43779 AA26247 A070337 A000017 BE396788 BE146000 A140003 A186951300 BE326763 A565133 T11443 AW191729 Z39644
 AW148267 R44776 W4028 AA133831 D81179 AW292596 W42633 A434033 A18674678 R33792 Z2006 A04212946 AW1665565
 W94015 AW51691 A183618 N02349 F03925 F13300 A23564 A183618 A183618 A183618 A183618 A183618 A183618 A183618
 A153554 A153518 A183774 A102025 AW00834 A18675256 AW06300 A088420 A50307 A1867527 A1867527 A1867527 A1867527
 A1865657 A1869986 AA22447 AA54152 AW066040 A070073 A4573096 A057436 A1071118 A093330 A14273819 A1692626 AW127648
 A4522067 AW134300 A00341 A124771 A1478720 BE139653 A1614032 A1241716 AWB14196 A2424116 AA424321 AA424321 AA424321
 A1857679 A1849575 AA506033 AW000765 A1825647 A1867711 A123686 A0037412 A1849576 AW1990633 A1868349 A1869113 A1869113
 A254582
 R44714 A1862896 A623116 A1271632 T10160 Z40966
 D06962 Z43779 AA26247 A070337 A000017 BE396788 BE146000 A140003 A186951300 BE326763 A565133 T11443 AW191729 Z39644
 AW148267 R44776 W4028 AA133831 D81179 AW292596 W42633 A434033 A18674678 R33792 Z2006 A04212946 AW1665565
 W94015 AW51691 A183618 N02349 F03925 F13300 A23564 A183618 A183618 A183618 A183618 A183618 A183618 A183618
 A153554 A153518 A183774 A102025 AW00834 A18675256 AW06300 A088420 A50307 A1867527 A1867527 A1867527 A1867527
 A1865657 A1869986 AA22447 AA54152 AW066040 A070073 A4573096 A057436 A1071118 A093330 A14273819 A1692626 AW127648
 A4522067 AW134300 A00341 A124771 A1478720 BE139653 A1614032 A1241716 AWB14196 A2424116 AA424321 AA424321 AA424321
 A1857679 A1849575 AA506033 AW000765 A1825647 A1867711 A123686 A0037412 A1849576 AW1990633 A1868349 A1869113 A1869113
 A254582
 R44714 A1862896 A623116 A1271632 T10160 Z40966
 D06962 Z43779 AA26247 A070337 A000017 BE396788 BE146000 A140003 A186951300 BE326763 A565133 T11443 AW191729 Z39644
 AW148267 R44776 W4028 AA133831 D81179 AW292596 W42633 A434033 A18674678 R33792 Z2006 A04212946 AW1665565
 W94015 AW51691 A183618 N02349 F03925 F13300 A23564 A183618 A183618 A183618 A183618 A183618 A183618 A183618
 A153554 A153518 A183774 A102025 AW00834 A18675256 AW06300 A088420 A50307 A1867527 A1867527 A1867527 A1867527
 A1865657 A1869986 AA22447 AA54152 AW066040 A070073 A4573096 A057436 A1071118 A093330 A14273819 A1692626 AW127648
 A4522067 AW134300 A00341 A124771 A1478720 BE139653 A1614032 A1241716 AWB14196 A2424116 AA424321 AA424321 AA424321
 A1857679 A1849575 AA506033 AW000765 A1825647 A1867711 A123686 A0037412 A1849576 AW1990633 A1868349 A1869113 A1869113
 A254582
 R44714 A1862896 A623116 A1271632 T10160 Z40966
 D06962 Z43779 AA26247 A070337 A000017 BE396788 BE146000 A140003 A186951300 BE326763 A565133 T11443 AW191729 Z39644
 AW148267 R44776 W4028 AA133831 D81179 AW292596 W42633 A434033 A18674678 R33792 Z2006 A04212946 AW1665565
 W94015 AW51691 A183618 N02349 F03925 F13300 A23564 A183618 A183618 A183618 A183618 A183618 A183618 A183618
 A153554 A153518 A183774 A102025 AW00834 A18675256 AW06300 A088420 A50307 A1867527 A1867527 A1867527 A1867527
 A1865657 A1869986 AA22447 AA54152 AW066040 A070073 A4573096 A057436 A1071118 A093330 A14273819 A1692626 AW127648
 A4522067 AW134300 A00341 A124771 A1478720 BE139653 A1614032 A1241716 AWB14196 A2424116 AA424321 AA424321 AA424321
 A1857679 A1849575 AA506033 AW000765 A1825647 A1867711 A123686 A0037412 A1849576 AW1990633 A1868349 A1869113 A1869113
 A254582
 R44714 A1862896 A623116 A1271632 T10160 Z40966
 D06962 Z43779 AA26247 A070337 A000017 BE396788 BE146000 A140003 A186951300 BE326763 A565133 T11443 AW191729 Z39644
 AW148267 R44776 W4028 AA133831 D81179 AW292596 W42633 A434033 A18674678 R33792 Z2006 A04212946 AW1665565
 W94015 AW51691 A183618 N02349 F03925 F13300 A23564 A183618 A183618 A183618 A183618 A183618 A183618 A183618
 A153554 A153518 A183774 A102025 AW00834 A18675256 AW06300 A088420 A50307 A1867527 A1867527 A1867527 A1867527
 A1865657 A1869986 AA22447 AA54152 AW066040 A070073 A4573096 A057436 A1071118 A093330 A14273819 A1692626 AW127648
 A4522067 AW134300 A00341 A124771 A1478720 BE139653 A1614032 A1241716 AWB14196 A2424116 AA424321 AA424321 AA424321
 A1857679 A1849575 AA506033 AW000765 A1825647 A1867711 A123686 A0037412 A1849576 AW1990633 A1868349 A1869113 A1869113
 A254582
 R44714 A1862896 A623116 A1271632 T10160 Z40966
 D06962 Z43779 AA26247 A070337 A000017 BE396788 BE146000 A140003 A186951300 BE326763 A565133 T11443 AW191729 Z39644
 AW148267 R44776 W4028 AA133831 D81179 AW292596 W42633 A434033 A18674678 R33792 Z2006 A04212946 AW1665565
 W94015 AW51691 A183618 N02349 F03925 F13300 A23564 A183618 A183618 A183618 A183618 A183618 A183618 A183618
 A153554 A153518 A183774 A102025 AW00834 A18675256 AW06300 A088420 A50307 A1867527 A1867527 A1867527 A1867527
 A1865657 A1869986 AA22447 AA54152 AW066040 A070073 A4573096 A057436 A1071118 A093330 A14273819 A1692626 AW127648
 A4522067 AW134300 A00341 A124771 A1478720 BE139653 A1614032 A1241716 AWB14196 A2424116 AA424321 AA424321 AA424321
 A1857679 A1849575 AA506033 AW000765 A1825647 A1867711 A123686 A0037412 A1849576 AW1990633 A1868349 A1869113 A1869113
 A254582
 R44714 A1862896 A623116 A1271632 T10160 Z40966
 D06962 Z43779 AA26247 A070337 A000017 BE396788 BE146000 A140003 A186951300 BE326763 A565133 T11443 AW191729 Z39644
 AW148267 R44776 W4028 AA133831 D81179 AW292596 W42633 A434033 A18674678 R33792 Z2006 A04212946 AW1665565

PCT/US02/17594

WO 02/098358

PCT/US02/17594

134444 32427_1
 5
 10
 127229 11897_1
 127236 19449_5
 134563_1
 20
 35
 40
 110930 127692_1
 45
 113402 9346_1
 127294_1
 104394 22054_0
 103739 17009_2
 133620 11876_2
 50
 129545 11897_1
 103797 109699_1
 133666 14685_1
 65
 70
 75
 80

BE184466 BE396167 BE105660 NM 003044 X04470 AE132992 AB62146 AB64623 AB67295 AB913549 AB22099 AB404343 X04503
 X04492 AB052192 AE114471 AB097001 AB186540 AB186545 AB186547 AB186549 AB186550 AB186551 AB186552 AB186553 AB186554
 AT428122 AA551906 AB226407 BE332000 AB303775 AA623166 AA587140 AD42206 AA838320 RT1534 AA326249 AB091599 AB3312654
 AE580185 AE100673 AW513394 HB5171 AB612494 BE612943 AB377093 AA035992 AE140713 AE594366 AD42358 A2E2099
 AB478909 AB126451 AW100276 AB510396 AB91397 AB066534 AB93550 AB127644 AB104603 AB026264 AB437678 AB1103736 AB026420
 AC31077 AB063022 AC347350 AB575769 AC300086 AB613709 BE160402 AB445434 AC302135 AE593536 AE593536 AB102481 AB132956 AB108445
 AW107008 AB35410 AB11543 AB116471 AC306669 AB729933 AB126232 AC27807 AB252818 AB178057 AB179057 AB179057 AB179057 AB179057
 AB64142 AB2632 AB164141 AB167398 AB168296 N2371 AB67529 AB6229636 AB16967 AB167153 T65335 BE181364 AB046628 T26664
 AC359779 AB464391 AA106226 T08493 AB36387 AB9912 AB74193 AB91207 AB17785 AB00077 AB740945 AB895649 AB145415 AB175381
 AB14529 AB565301 AA109179 AB1091622 AA485776 AA485649 AB910051 AB91248 T28 AB65920 AB59965 AB86793 AB474907 AB30365
 AE40664
 BE139545 AC200503 BE169249 AW063101 AW063101 AC043699 AA370199 AD4032221 AB651339 AB119742 AB02228 AB164070 AC394574
 AA995977 AC032279 AB079284 AA513174 AA083121 AC045179 AA483363 AA528432 AA579511
 AW066187 AE15426 AB34181 AB120457
 NM 013233 L35635 M06844 A950516 AA434132 AB495745 AE580161 AA594222 AB465587 AA275036 A909743 AB465587 AB145262
 AB190051 BE17435 BE164574 BE002291 AB27505 AW176047 AB048549 AB097001 BE090680 AB677897 AB475768 AB343803
 AC055735 AW574574 AB365230 AW075573 AB103035 BE148067 DE000610 AW510559 BE002441 AW173702 RA5919 AW53774 AW1372169
 AB107139 AW57319 AB233381 AW536508 AW033501 AB249672 AW076020 AW063674 AW599345 AB362098 AB164354 AB367166
 AW073218 BE000689 D07567 BE16434 BE022086 AW069725 BE045675 W03587 AW061129 AB85465 AA445851 DE1591 AA441171
 AE525208 AB71144 AB058499 AB450407 BE173584 AB137311 AA255400 AW051190 BE020075 DE4338 DE4370 DE3686 DE3636 DE0601
 DE4567 R2342 AB766490 DE2634 R23767 AB100088 AC262280 AW151336 W06964 AB165308 H02424 T1654 BE12502 D51201
 BE125228 DE5311 BE000449 AA300121 AA523877 AA430455 AW392680 AW392679 AB100652 AB26053 AB100671 AB10781 AW08838
 AC050029 AB171845 AE55712 BE059791 AB472954 AW151628 AB472990 AA045184 AB120238 AB510250 AA31438 AW150119 AB136006
 AW162098 AB457572 AB122055 AB0655310 BE545665 AB661407 AB474396 AB467619 C05711 AB10611 AB294745 AB59440
 T467675 AW101199 AB43531 AB5284 AB429640 AC229021 AC208414 AB27244 AB279487 W03816 AW47071 AB10589 AB20365 DE0601
 AW546403 AB27182 AE126065 AB49869 BE219021 AW265621 AB245637 AB56105 AB257041 AB67736 AW12506 AB144845 AB44455
 AE526301 AB597327 AB796682 AE527859 AB511997 AW005027 BE179026 AB500230 AB10148 AB595396 W0475 AB044857 AB237655
 AB534433 AB116541 W73522 AB051471 W73531 AW043384 AW024728 AB66840 AC00094 R77739 BE0549 AC209450 AB47739 BE75799
 AC205687 AB165307 AB118765 H02405 AW191786 AW041533 AB157340 AW473548 AB375396 AW172099 C73585 AB55826 AB370378
 AC302305 AA435555 A5973160 AD244703 AE57165 AW272161 AB207746 AB206035 AB340107 C75151 HB9116 AE52273 AB353039 AB395764
 AW087507 AB69500 AB04470 AD28216 AB01366 AW062195 AB056877 R23736 BE153112 BE139490 AB91452 AB1692452 BE152446
 AB007735 AE53371 AB154940 AW102555 BE165971 AB1732914 AB1732914 AB17007369 AB19791 AB05282381145709 AB971065 AA465730
 BE45455 AB171980 AB172946 AB17427 AB096163 AB171980 AB171980 AB171980 AB171980 AB171980 AB171980 AB171980 AB171980
 AB091817 AB103161 AE142444 AB440317 AB059162 AB027948 AB027948 AB027948 AB027948 AB027948 AB027948 AB027948 AB027948
 AW157352 AE539146 AB24403 AC302687 AB033621 AB27336 T03913 AB676303 AB107099 AB15702 AB75491 AB977101 AB37336 AB107452
 AW490010 AB202938 AE558862 AB169929 AB569007 T03653 T03024 AB662348 AB455981 AB1081834 C20119 AB11355 C25654 AB910304
 AW119061 AB867539 AB024794 AB093574 T03912 T03652 BE002321 AB71466 AA465334 AB194350 AB193302 BE176743 BE004975
 BE274545 BE074891 BE020606 BE175765 BE13347 BE001166 DE58707 BE020111 BE175845 BE000504 AB099854 AB432001 AB434529
 HB9195 AB357314 AB123763 AB123763 AB123763 AB123763 AB123763 AB123763 AB123763 AB123763 AB123763 AB123763 AB123763
 AW350006 T00552 AA349976 AB610643 DE000015 AB766762 AA301304 AB474775 BE160467 AB105002 AE121404 BE17402 AB373663
 BE274545 AB764850 AB376799 DE45438 AB384504 AB384504 AB164151 BE1453 D59504 AB653090 BE273565 AB47306152 AT57811 AB1 A597010
 BE1510
 BE242991 AB470094 AD242879 AB367403 AB103570 AW1051712 AD4059667 AB149027 AB5403 AB5403 AB5403 AB5403 AB5403 AB5403
 AD071703 AB27302 AB6603 AB51216 AB704040 AB193579 AW0003140 AB704043 AE42195 AB390397 AB192299 AB1970 AB144442 BE140136
 AD241459 AB14574 AB6694 AB6694 AB6694 AB6694 AB6694 AB6694 AB6694 AB6694 AB6694 AB6694 AB6694 AB6694 AB6694 AB6694
 X54942 NM 101627 AB145936 BE595311 AA252664 AB119862 AA240011 AA306157 AC425268 BE565891 AW172736 AB764904 AD19784
 AB147590 W07386 R00555 AA44487 AB155521 AC20261 AB10006 AB107445 AB278555 AB278555 AB278555 AB278555 AB278555 AB278555
 AW327300 HB9393 AB172911 AB4729539 D19359 AA234002 W15179 T26560 AA305796 BE154003
 AA129551 H46857
 AB115173 AD075221 AB075709 AD075354 AB083101 AB083391 AD070584 AB063386 AB076395 AD076395 AD075791 AB053600
 569651 S93503 AB13385 AB102121 AB103548 AB401449 X03635 AB470222 AB2512813 AB262696 AB102555 AB149147 T5352 AB448018
 AW072003 AB06774 AB439323 AB069402 AB480490 AB053265 AB151424 AB151424 AB15334 AB15334 AB15334 AB15334 AB15334 AB15334
 T52701 AB145974 AA457690 T30216 T30226 AB75183 T63495 AA487181 AB872156 AB72305 AA487096 T30224 AA487096 AB37025 AB358623
 AE430447 AB638970 AW127149 AW262236 AB630516 AE457450 AW270564 AA486039 AB970112 BE324652 AB299636 AB46546 AB634025
 D45957 AB62696 T63633 T63636 T64546 BE5979
 AB15101 BE43545 AC200503 BE169249 AW063101 AW063101 AC043699 AA370199 AD4032221 AB651339 AB119742 AB02228 AB164070 AC394574
 AW995977 AC032279 AB079284 AA513174 AA083121 AC045179 AA483363 AA528432 AA579511
 AW080012 AD075718 AB083403 AB075594 AB076992 AD064526 AB406181 AB113913 AA113382 AB063021 AA134501 AD062953 AD070343
 AD052335 AD075435 AE532593 AD071252 AD078000 AD064526 AB0974305
 AB15101 BE43545 AC200503 BE169249 AW063101 AW063101 AC043699 AA370199 AD4032221 AB651339 AB119742 AB02228 AB164070 AC394574
 AB454510 AW063205 AW066299 H7670 AB35859 AB091818 AB091818 AB091818 AB091818 AB091818 AB091818 AB091818 AB091818
 AW165168 AB061552 BE407187 AB0615423 BE460953 BE254698 F13473 T47411 T69894 BE296466 BE299756 W72745 W00481 AB77387
 AB107139 AB72636 AB74056 AB453176 AB249789 AB365011 R22482 AB990515 H76398 W73493 AB631187 AB659369 BE363435 T05074
 AB199150 AB98162 T46533 R23686 AB002749 BE222599 AD064227 AB100247 AB36698 AB10046 H63312 AB74966 AB150880 AB192513
 T269700 T08619 AB049740 AB102191 AB102191 AB102191 AB102191 AB102191 AB102191 AB102191 AB102191 AB102191 AB102191 AB102191
 R72745 AB76870 AB76870 AB76870 AB76870 AB76870 AB76870 AB76870 AB76870 AB76870 AB76870 AB76870 AB76870 AB76870 AB76870
 BE026585 AB16350 AB17673 AB1145001 AB049163 AB081661 AB355536 AE221419 AB058982 AB1188675 AB193368 AB33700 AB10674
 AB358523 AB4888 AB4645 AB077669 AB43384 AB0808 AB09130 AB055309 AB047617 AB169564 BE074249 AB31310 AB040341 AB1193681
 AB15475 AB126750 AB202682 AB454375 AB102191 AB202682 AB454375 AB102191 AB202682 AB454375 AB102191 AB202682 AB454375 AB102191
 AB551591 AB184897 F14021 AB259210 AB259210 AB259210 AB259210 AB259210 AB259210 AB259210 AB259210 AB259210 AB259210 AB259210
 W79109 AB527708 AB79472 AE59148 AB60146 AB602641 R26660 AD02219 AB022595 AA367691 AB34361 AB15533 AB15336 BE05882
 AD40749 AB14616 AB146353 H44276 R25042 AB140047 AB140064 AB146596 AB051533 AB15533 AB15533 AB15533 AB15533 AB15533 AB15533
 AB104718 AB51354 T04667 R1905 AB10912 AB093038 AB13483 AB13483 AB13483 AB13483 AB13483 AB13483 AB13483 AB13483 AB13483
 AB43459 AB10160 NM D03234 BE26019 BE14289 BE14279 AB050505 AB050505 AB050505 AB050505 AB050505 AB050505 AB050505 AB050505
 AW063024 AA025588 AA216654 AB002703 AB07771 R22031 N56217 AB134422 AB021417 AB133990 AB021417 AB133990 AB021417 AB133990
 AD463375 AB088721 R58492 AB149843 AB13210 BE092247 AB11866 F05413 N85500 H60074 H02305 AB059482 DE0985 R82712 AB1004269
 BE03373 AB12168 AB0954 AB0954 AB14181 AB14181 AB0954 AB0954 AB0954 AB0954 AB0954 AB0954 AB0954 AB0954 AB0954 AB0954
 AB400725 AB51154 AB51154 AB51154 AB51154 AB51154 AB51154 AB51154 AB51154 AB51154 AB51154 AB51154 AB51154 AB51154 AB51154
 T64396 F0003 F00134 AA273609 W02336 AC005505 AB665937 T30304 ABW72879 T29785 W34700 R0458 ABW7290 ABW15197
 AB0954 AB12168 BE090622 BE090615 BE090616 AB630083 AA010798 AB1030222 AB04713 AB1075430 ABW75585 BE05329 AB093505
 AA042741 BE092490 AB30297 ABW75916 R36193 BE09288 ABW75696 D20702 AA262852 H04165 R29433 ABW7584 ABW75175 AB06223
 AD595714 T3197 AB2895 AB06164 BE042743 AB740874 AB108806 ABW168040 BE220522 AA521414 AB191327 AB173980 AB160417

CT/US02/17594

13

PCT/US02/17594

CT/US02/17594

1

PCT/US02/17594

PCT/US02/17594

PCT/US02/17594

1

1

WO 02/098358

PT/US02/17594

[illegible]

PCT/US02/17594

14

WO 02/098358

PTC/US02/17594

					AB09711 AA514515 AA32034 AA464102 AA59950 AA74349 AA56025 AA292187 NB0101 AA29392 AA641245 AA192049 AB082031 FB04187 FB726 HB0491 AA30203 AA22204 HB0633
	100114	17101_2			XQ2308 NML_01071 FE389795 FE280576 DE27111 FE254747 D00596 BE307212 T90837 AA022734 AA022734 AA011908 T30265 AA33400 AA324075 FE458746 AA026518 AA174883 AA146605 W21187 AB567436 AC39850 AB198482 AA43193 AA140108 AA000495 CT1075 BE329762 AB192518 AA514981 AA3008921 AA175911 AA271781 AB155570 AB41436 AB196301 AA54837 AB03407 AA476948 AA105735 AA11609 AA74208 AA143538 AA27855 AA47675 AB05867 AB05867 AB177673 AA112870 AA740553 AA476309 AB02400 AA075379 AA17413 AA070391 AB14714 AB53744 AB041387 AB08444 AA12584 AB046601 AA24790 D22012 AA09353 AB04740 AA63310 AA248117 AA65664 BE35555 WB0607 WB6539 NB4557 AA174823 H74065
	100144	13999_1			AB119954 AA160379 AA401219 D13645 AA58185 AA5962124 T82834 AB027754 DE077738 AB135438 T06133 AA081208 AA599623 BE297541 BE257304 BE253389 BE059086 BE060635 AA243118 AA284790 AA002869 B510255 AA249641 AA104897 DE725559 FA225955 AA094138 AA426402 AA020418 BE331233 T10765 AA0202 DE229672 BE312815 AA174044 AA07985 AA34811 AB1929475 DE274623 BE314908 BE304719 AA173117 AA345770 T1525 DE514631 H27789 AA113008 AA349104 DE272501 AA081634 AA572770 AA0 HE2576 AA35374 AA050003 H10011 DE514639 AB314948 BE271929 BE272003 W32723 WB9455 AA155977 HE2693 BE272251 AB133557 U125940 W1931 AA482423 AA440047 BE6733 BE272820 AA489291 AA373562 AA150651 BE314798 H181348 A110641 AF063521 AA080933 H19959 H53210 BE33634 AL047117 F1261 NB0409 NB0391 T5057 BE320272 BE232455 WA024 AB547249 AB270753 H0001 FE302291 NB7838 H53340 H42025 H63348 W192108 AA489271 AA439815 AA41915 BE277158 AB06589 F03331 AA43733 AA515157 AA177383 H38996 H48225 AA267070 AA36280 NB2919 H20330 AA501746 AA37943 AA594748 BE392141 AA094742 AA594745 T73126 AA594748 AA594745 AA40508 D54907 AA749901 NB4300 R08916 W20481 AA333707 AA029503 AA305667 W52768 H13395 AA349028 AA482524 T6392 FE394527 H47443 AA173221 W63260 D20420 W5248 A120991 AB71394 A150998 AB09982 AB09755 H39306 AA420214 T67690 AA271719 AB54768 H437311 AB71368 AB1274 AB09376 AA248437 AB09171 AB277158 AB06589 F03331 AA57753 AA026901 H146289 AA483472 AA02572 AA105451 AB070645 AB079113 T47472 AA373651 A160997 AB7036 AA026722 AA152112 N21356 W46558 AA136070 NB7878 CO0484 AB32700 AA065796 AA4732843 AA428655 AA586004 N5782 A1307238 H63632 AA192904 AA854322 A1346385 AB92304 AA064755 AA482228 H47353 AB718548 AB730473 AA264035 AA070539 AA570505 AB0277 HB0331 AB037114 D19254 DE2262 AB56744 AD07117 AA115187 AB70839 NB5281 AA247088 AB03601 A170228 AB0851 AB3385 AA117106 AB27533 AB56770 AA42934 AA02540 AA01291 H659327 WA4489 AB70628 R08719 A140171 N27013 A112670 AA033613 AA1032977 WA7339 AA429268 H71431 WB4804 AA724616 AA119594 AB744207 H67506 AB148115 T2851 AB700564 W95151 AA15662467 AB31421 AA1301 AA128918 H98440 DE221002 AA947246 AA349234 W04138 AA745222 R30953 AA800676 AB67781 H75835 AA540201 AA174758 AA543415 AA689328 F10463 D29855 AA341914 AA78306 R62021 AA348227 H63321 H70321 AB204737 AB380442 AA547013 A2716689 AA34165 AB77369 AB31312 AB133222 AA0558 AA05186 AB11981 AB71332 AA433152 A140281 AA281188 W47216 AA579228 AA611994 T61892 N10359 N185338 H41267 AA773356 AL042978 BE51138 BE364988 H70222 HB0840 H71430 H53315 H70320 H75271 NB00791 T71383 R13414 C00137 AS157553 BE32606 BE305235 AA994771 AB7094748 BE394341 R62294 AA541545 AA342977 AB05938 T12538 T7943 AB4546 BE300736 BE332234 W16025 H00536 T62613 AB054343 N99465 T61896 A380215 H477661 AB69122 H5256 AA37006 AB05930 T21443 BE33074
	100154	16656_1			H0720 D14667 NML_014738 BE357098 BE3596112 FE709691 AB040480 AA034707 BE564467 BE565224 DE567003 AA36693 AA326057 H40371 F01106 AA330795 BE546676 AA315764 AA352277 H63720 WB8219 H670726 AB273497 AB332526 AB39837 W4242317 AB192481 AB101413 AB19304 AA400655 F91107 H59445 AA40616 AB14038 AB344272 AB58250 AA79430 AB726716 AA0629318 AB33951 AA339632 A219469 AA038837 BE200212 BE613561 AA530135 AA350343 AA299704 AA615256 AA326066 AB380114 A138555 F08643 A1195922 AA076009 AA847389 NB2220 NB2871 AA644547 AA041660 AA23202 AA77953 AB084652 T2083 AS38747 N02534 AA359635 AA00746 AB04140 AB004745 AB11961 AA487232 DE0432 BE267841 AA799111 H06951 R70296 NB0819 H17007 H07025 AA32708 R37006 H40318 NB4253 BE587446 AB655330 AA054794 AB105004 R36629 AB03647 AB778075 AB310288 H73444 H73505 WB0887 H04688 D14874 NML_001124 AA011272 W71357 F08781 D2811 R08871 C17011 C17019 A7151223 DE273115 AA25156 AB0486 AB203523 A1511224 R3308 H0950 H47186 D4330 573006 R0357 AB1149 AB77802 AB778014 AB56571 A128041 AA731484 AB054651 AB00389 AB04640 AA11172 DE273450 AB741960 AA338964 AB2481 AB10921 AA72915 AB10441 A338209 A233631 AB69239 AB080311 NB2613 A120873 A1655206 AA051900 AA02337 AA874623 N20993 AB39337 AB02454 AA583015 A023730 A151225 A1200677 A1373369 AB35369 AB540560 AA192411 AA46120 AB07450 A75243 AB2543 AB286425 AB23790 AA335868 A71457 AB45667 AB644428 AA319343 A261791 AA124069 AA830748 AB071978 H01326 AB74374 N2557 AB70456 AA470391 A717659 W19284 AB2843 A16819 AB70377 AB39704 AB26328 W35476 AB02744 H64045 AB103892 AB08140 AB380134 R05098 R06085 R05037 AB09591 H10951 A105135 AB07654 R0068 AB389219 AA017304 AA009795 AB06975 A18361 AB103771 H42161 F05088 BE1586 AB68996 N2576 AB504118 AA50440 AB52361 AA886325 A1353573 F05462 AA319198 AB85800 AA070521
	100187	15823_1			AD02481 AA422691 AA027790 N27217 N26931 H24806 A02108 DE265900 N7945 BE544892 R3317 R26474 H1793 AB01860 AB110349 BE22698 AB57236 AA421535 W3436 AB02306 BE58465 R0828 AB580626 W19890 AF140116 NML_016253 AB565223 T67368 NML_003703 L40838 W21407 F08737 F05676 T17306 F06300 AA336431 BE30114 H6896 W06260 D4812 DE2312 AA366446 H73624 AA063269 T27869 AA095005 AA203134 DE002352 W4844 AB517544 AA042153 H24611 AB196306 AB94756 T27884 AA543129 AB31673 AB197401 A273556 AB501614 WB0223 AA02840 AB041939 AB48667 AA00496 AB566150 AB09330 AA147163 AA147070 AA552784 AA557378 CT5304 AB749277 A270892 AA08558 AB06549 AB19921 AB362429 AA82761 AB050004 AA708622 AB24609 AB74156 AB11892 AB4545 AB11892 AB4545 AB11892 AB4545 AB11892 AB4545 AB11892 AB4545 AB11892 AB4545 AB14714 AA46778 AB38187 AB00736 AB06927 A27275 AB05021 A916325 A010717794 AA78222 AA58244 AB001704 H52471 A123388 N00416 AB192013 T67421 A2161978 AA043631 ABW13665 AA572719 A127780 A025010 A022915 A11720 A1270338 US9439 AA14704 A126309 H04497 AA116886 AA008843 AB703857 AA590227 AB17684 C0641 AB0515 A020840 W05956 H63937 R2154 AB50421 A265164 AB50528 AB05265 A075141 W0506 H6296 W0648 W06501 F33098 H57878 AB352266 W15361 T47402 AB24316 H0506 AB06500 W27792 C06427 W04638 H74675 AB02895 F046722 D57312 AB078198 H42732 CT5304 AB06589 AB781648 AA0484781 F02592 H73625 AA524157 A250707 BE260237 AB565823 BE17020 AB706809 BE11951 AA53507 DE30426 BE66782 T18027 T47032 AA47104 AA04481 A245341 BE69892 W35320 F05676 R85439 DE58238 A101414 AB56687 AB4872697 AD02693 A269233 W5377 BE59588 AB77255 AB58049 T74425 AB74923 AD7352 AB01498 AB043484 AA009509 AB07320 AB073536 T67238 AA091194 AB46259 T3148 T2521 AB59389 AB05196 AB46550 T4919 BE06476 DE56811 AB53860 AB59620 DE58296 D25218 DE206506 BE38961 DE38799 BE367932 DE360034 AA100812 AA100056 AA147503 AA347329 AB702757 AB444723 AB891104 AB53248 BE048325 BE185154 H21250 H22075 A0552129 AB29730 BE183526 AB218256 AA01528 AB471485 A190957 AB747449 AB47148 AB25211 A1100813 AB59555 AB73665 A332995 AB76536 AA78769 AA516400 AA50476 A152497 AA440293 AA53007 AB05817 AB05817 H2209 AB06130 H20295
	100199	12561_1			AA479005 AA291991 AB71781 AB78117 AB74248 AB740162 NML_003311 AF001294 AF01458 AA83725 AA008415 A1290356 NB0811 R09174 AB26233 AB015740 H08878 AB039294 AF019563 F75643 AB741008 AB741269 AB18888 AB077833 AB321621 A766645 A129104 AB077671 B738609 AB41143 A337297 A277233 A565240 AA22619 AB283320 AA693675 AB051978 A10219 A192135 A028196 AD29332 AB6924 A7647215 H29541 AD200143 AB02423 AB0984 AB98429 AB084497 AA051796 A112290 AB2248 DE19424 AA53327 AB47762 AB07274 AB098971 AD76577 AB02213 AB0616 AB2357 AB09192 R2062 AB05669 AB143140 AB476061 AA797656 AA365304 T35135 T36140 T35143 D20894 AB11274 A1059265 AA147723
	122411	30018_1			AB712356 A232077 AA446868 AB432375 AB67144 AB274018 AD28165
	129417	29608_3			AA146828 AB88288 AB34335 AB71788 N551734 AB51734 AB51741 AA570997 AA425746 AB78618 AB563305 AB034848 AA428659 AA431328 H01728
	115291	23235_1			BE545072 AA50759 AA301103 AB106175 NB5422 BE563965 AA327978 AB16094 A0001515 BE01319 AB279943 BE13895 AB487845 AB963051 A00029 AB283962 AB53752 AB59007 AB18135 AB56636 BE501307 AB272785 AA042236 AB788315 A0145427 AB57486 AB354483 AB74045 AB056739 AB973322 AB92180 AB472921 DE504748 AB32998 AB500706 AA769228 A1370582 AL137710 BE003656 AB065920

PCT/US02/17594

WO 02/098358

PCT/US2012/17594

A228444 AA503911 AA565282 AA585335 AA574401 AA224941 AA652562 AA640688 AA652767 AA935442 AA641051 AA228914 AA934464
 AA467738 AA469190 AA506584 AA226574 AA654984 AA574741 AA595875 AA572622 AA654984 AA574741 AA595875 AA572622
 AA225688 AA578333 AA533825 AA579236 AA580806 AA206974 AA658203 AA488477 AA229966 AA553375 AA589449 AA541337 AA388317
 AA681841 AA596953 AA567879 AA505019 AA553343 AA587824 AA548855 AA687194 AA540120 AA569708 X76882 AA559295 AA532441
 AA559520 AA533637 AA201973 AA069642 AA174893 AA526834 AA224543 AA648070
 AA223535 AA573045 AA947375 AF151675 AA227284 H6E477 AA585052 AA592355 AA206981 AA558979 AA584593 AA613499 AA617721
 AA464475 AA624049 AA436551 AB126208 AB161070 AA055010 AA048714 AF151019 AA489866 AA561879 AA684491 AA126238 BE263495
 AW974670 AF161600 NM10131 XW3698 AA567709 XW6039 BE387895 AA230309 AA152012 BE613491 AA151760 AA157416 BE260699
 BE131477 AA625533 BE154747 AA657391 AA105046 AA081899 BE410812 BE138275 W16726 AA369472 AB3027 AA557345 AA1188258
 AA372444 AA565436 AA187417 AA152096 AA934226 AA084496 AA000707 AA572294 AA810270 AA080000 AA362844 AA612637 WA9299
 AA323575 AA552696 AA010286 AA111122 AB111113 AA547077 AA158529 AB887242 AB222141 AA386699 AA373636 AA561077 WA9299
 AB661750 AA715119 AA169767 AA532477 AA206061 A1193562 AA202676 AA504914 AA235730 A1150428 AA4766630 AA859400 AB66620
 AA533724 XW9014 AA617906 AB189522 A2184283 AA845651 A302333 X759662 AA548855 XW0127 AA410400 AA03167 AA564451 AA507614
 AA389895 AA860762 AA516287 AA5070106 A7760657 AA251834 AA243306 AA384045 AA465636 AA069966 AA1768338 AA627255
 AA452761 XZ9361 C03037 NM104116 XG65151 X7096 AB38168 W740 A4131953 X00267 AA563584 AA553399 BE44151 X29632
 AF173891 AA535392 AA32461 X23876 A277239 AA133035 AA070285 AB7620 A4756952 AA55209 AB384159 AA53502 A27296 AA242942
 A242927 AA549705 AA0570171 T65049 AA831475 F09516 AA00051 N57454 AA206400 AA347304 AA445029 AA565732
 U81902 LA134741 AA283696 AA27592 AA28208
 AA369601 AA3470114 BE163589 WA4625 C06870 F46424 AA563692 AA591362 AA514300 NM1005746 UC0200 F06445 AA282449 N47287
 AA467996 APT54526 APT54567 APT17855 APT54542 APT18027 APT17852 APT17882 APT14798 APT54567 APT17852 APT14798 APT54567
 AA098116 BE1638 AA344546 AA344115 AA006022 BE920411 AA345021 AA65448 AA5414 A1133596 AA349695 AA991265 AA2363420
 L2N50 AA528246 AA296240 APT38995 A2091110 AA570106 AB37489 AB21237 AA330246 APT03011 AA91216 AA510844 AA321466 AA116949
 AA130031 AA326784 AA0713546 AA059153 A1W747906 XW6346 AA570306 BE161948 AA117164 AA417651 AA505971 X21013 BE404116
 A272354 AA03402 AA378189 AA056552 XG50820 AA227842 A220735 AA347110 AA262032 AA560001 AA467206 AA591314 AA596900
 AA307059 AA335693 BE44094 AA7081674 BE429153 AA17969 X30794 AA0511862 AA51358 AA000380 BE164688 AA112505 AA12508
 APT09227 D77867 AA796011 AA116659 N86700 R72589 F27284 F0228 X88264 D20542 AA087074 AA35416 AA067622 APT47240
 AA255720 AA510528 BE40585 AA371506 AA051170 APT1494725 APT230058 AA422955 BE405273 APT67033 AA84186 AA051077 APT36572
 APT1805 BE360421 AA60574 A551047 AA468381 AA326915 AA630993 AA436938 AA116928 AA534783 AA680075
 APT174857 AA16916 X5 A252828 AA468532 AB1068 F61335 A222396 AA538572 AA52566 AA210126 A21044 AA16906 AA594385
 AA341153
 AF121577 AF24684 NM100349 XH4373 X645706 AA687317 BE082476 BE082541 AA779730 AA147324 AA97761 AA62996 A2819515
 D82208 D82512 D82402 D821492 AA046193 AA311625 T65486 X91768 T65476 F11930 X42698 AA118908 AA458002 AA653072 AA557325
 R53543 AA334748 AA206780 AA525522 AA475984 AA240412 APT180896 AA65777 AA070780 AA449520 X73010 AA219119 APT201980
 APT11295 AA4454 AA41470 APT47464 X75900 X52544 X75912 A301350 AA494000 AA049086 AA208104 AA098696 AA20406 X24005 F05760
 AA4404101 AA197032 AA280832 F05647 AA516155 AA437306 BE241176 AA376408 APT753161 R17456 AA339004 AA95281 AA999119
 T02781 AA458303 X224852 AA305767 AA442395 X73099 NA5104 AA054374 X19164 AA529649 AA004825 AA299883 AA061785 BE358413
 APT18296 AA53625 APT271632 AA561890 AA895278 AWT247 AA3 AA664423 AA08968 AA084306 A526944 AA510033 APT72289 A208099
 AA347426 APT20201 APT50785 APT1132 AA46546 APT07002 AA405406 APT272171 AA540526 APT87186 A564551 A56264 A29521 X75780
 APT0217 APT730874 APT8211 AA176545 AA437465 APT5158 AA497620 X23592 AA388749 T65412 X50216 D81782
 AA393569 AA91632 NM101449 US5863 AA877669 AB30051 A30054567 AA57313 BE004116 BE004172 APT05701 AA75946 AA900183
 BE179065 X73259 APT16764 BE0281 X25 AA941878 BE081243 AA5751717 APT176761 APT176761 APT015013 APT015013 APT59440 A269226
 A551823 APT02867 AA552303 APT03700 AA510223 AA00066 APT35067 AA017130 APT173852 APT60233 A306993 A1392845 APT16076 APT02401
 APT72471 APT569715 APT014885 APT00626 AA026236 AA05154712 APT510116 APT51015 APT42200 BE51859 APT6522 A345320 A355300
 C1BE67 AA44721 X1 XW36450 AA448780
 APT067000 APT090201 AA497040 NM1003714 AF084642 AF056480 AA411788 H68195 AA097894 APT40274 A8021266 AA068334 BE219475
 AF051036 AA156435 AA597115 AA465344 APT673399 AA5229835 APT068230 APT373922 AA520016 APT371682 AA463458 AA610136
 BE119547 AA452343 AA525224 APT23204 APT260085 AA704668 AA69001 AA463301 AA0616145 W46426 APT08085 APT5149 APT6703
 HPT088 AA120990 APT067177 APT024572 AA126474 AA065770 AA113396 AA223369 A309075 BE213311 R15002 AA596075 AA3405041
 AA601338
 APT053005 AA046078 AF04741 AF043294 APT52692 APT00073 APT061961 APT137187 R94348 BE27005 AA338290 APT6959418
 AA501178 AA504435 AA515553 AA553294 AA400692 APT67064 AA585042 AA561452 APT571307 APT573277 AA313888 AA44501 AA567063
 APT05242 AA145452 APT029219 AA516327 AA540980 AA464393
 APT038786 APT69447 BE189022 BE297137 X205126 BE003963 AA596580 AA349464 AA351821 AA492538 AA6146232 D5158 APT001199
 R43589 APT732764 BE16807 AA062348 AA1160949 APT020721 T18538 AA161281 AA14349 APT72873 D80801 A871301 A1460100
 APT136252 APT71208 APT071873 AA431911 AA537838 APT06252 APT67027 AA083854 AA678651 AA411806 A335812 APT7199304 APT150270
 APT09098 T08931 AA54545 AA33061 D80910 APT158736 X394948 APT4381 AA534543 AA51620 AA4150 APT01782 APT06269 APT6369
 APT702382 AA376185 AA049462 AA355733 AA102438 AA1006 A4032521 AA425180 AA58968 H50482 A362525 XPT41 APT307160
 W89036 APT05827 APT50044 AA102418 BE89918 APT33305 AA551928 APT082735 APT189962 A557485 AA505920 AA494149 A422826
 APT08299 AA343408 AA043409 AA036488 APT043036 AA677114 AA176237 AA1811893 AA0026405 H63534 APT02015 X789936 APT160217
 APT365349 A31453 XPT518 BE2821 AA060717 H41545 AA15808 AA10349 AA089535 AA054523 BE1594 AA20178 APT05768 APT6269
 AA64017 APT04650 AA454885 APT00271 APT61671 APT50709 APT04669 APT61127 APT072027 AA47132 APT01227 APT01227 APT11 APT4219
 APT00201 BE305115 BE244257 APT313957 AA354345 AA4811981 AA672091 AA482098 AA441318 APT6136 AA004345 AA66537 AA05682
 APT01227 APT038172 T77206 AA0675061 APT060758 AA518287 T39226 APT0723 A262765 APT062048 D81717 AA830290 W16962 T39468
 R67725 APT5181 AA539568 BE000987 AWT1326 APT18878 APT677326 APT40762 APT69551 AA145448 APT119835 AA90290 APT69576 APT69202
 APT68445 APT5389 APT6908 APT16732 BE5658 APT0030 APT6908 APT2881 APT2881 APT19125 T134333 APT15136 AA516716 F08449 H6814
 AA034991 AA46922 AA65356 AA386252 AA564135 R71484 APT214329 T24555 AA214170
 X00549 NM100911 X00548 NM100599 X00578 X00549
 APT49230 AA627843 AA584078 AA626529 APT043894 A44598 APT606653 AA136894 AA533945 APT029561 AA096114 APT168575 A4291513
 AA767321 AA067676 H66656 AA063644 APT079307 AA652435 XG5356 AA20025 APT032404 AA094135 APT032404 AA6117
 APT76901 AA191549 AA461615 X20832 AA4435217 H4336 H68021 AA445400 AA002584 APT6186 APT139578 APT6786 H6800 H6803
 R4455 APT362764 APT04802 AA249363
 Y09763 Y05737 NM104661 U06661 H07883 AA347289 BE001800 T78142 AA295632 APT147469 X60226 R64082 H63086 AA989734
 C17768 H63934 APT63394 H63732 AA6352 APT2325 APT3341 AA000993 APT01421 APT41987 APT070077 APT716409
 APT76857 APT7767 F05677 APT01676 AA682289 APT074433 T27014 AA00465 AA334196 APT5454091425 A418849 APT67980 AA354042
 APT24717 AA321214 APT67525 U28263
 NM101413 AA023493 AA55055 T27132 R00088 T51728 AA367536 APT372030 APT481069 X00266 AA099545 AA033736 AA011878 A145981
 APT015212 AA013384 T27131 BE463032 AA083737 AA664296 AA387347 W67623 APT606289 W91397 APT13977 T15308 BE46545
 AA137426 AA480180 AA450176 AA602166 W6736 A30416
 AA588572 AA101262 X00026 AA565938 AA332399 AA553360 NM100006 NM1369 APT14588 AA653326 T61867 APT276926 NM13636 T67969
 X77464 APT661653 AA652893 H68642 AA106973 AA106820 AA461959 APT612031 AA42037 AA33043 AA3236 APT50226 BE55229 X047137
 APT04929 AA117809 AA590068 AA565890 AA565890 APT3118 BE000635 AA517240 AA166922 AA833639 APT87338 APT46874 APT447122 APT21934
 H68554 X67306 BE439433 T29653 AA564943 BE065133 APT673276 APT1694 APT1694 APT38150 APT29226 APT172005 APT47209 APT47209

PCT/US02/17594

•

WO 02/098358

PTC/US2021/7594

AA514046 A342623 P29905 H20999 AA757144 H21636 F22104 AA422650 F27143 F26346 AA536990 H45771 AA548851 AA170154 H45646
H62211 AB21614 AA7581 AA57724 AA571408 AA544439 F22856 H41129 AA571805 AA571805 AA571805 AA571805
AA328523 AA523709 AA336448 AA375406 H46976 R68060 H02722 AA230321 AA328205 R62558 AA373727 AA304138 AA304224 AA301163
H54867 AA347783 AA567232 AA373239 AA374011 AA375673 AA330857 AA370465 AA378461 AA302613 AA304002 AA301731 AA375988
AA303326 R25744 AA301567 H78746 H20608 AA595423 RA7960 AA425456 AA001308 AA126411 AA729223 AA080271 AA913845 H26296
AA733335 AA342591 H27356 H26390 AA122615 R69996 AA730878 H292292 H16650 AA551125 H25944 H27514 W01159 H244285
AA176730 H180494 H28785 AA182958 H27795 AA232164 AA328344 H51885 H61804 H44544 AA571805 AA571805 AA571805 AA571805
AA262164 AA139474 AA139476 AA001045 AA614374 AA593153 F33347 F34679 H66225 N25703 AA186999 AE23313 F13131 W27069
AA003161 H36146 H28672 AE80529 AA128960 AA259183 AW708696 F17446 F30433 AA303884 AA303867 AA303868 H26320 AA592479
AA027222 AA046482 AA591447 R53711 AA594976 F78704 R36689 F163221 H08433 AA280786 R53415 H45716 F37346 H492445 AA3362679
AA30815 AA375442 AE71376 F37894 AA33874 F73579 R62478 F59400 AA088625 AB267590 AW71675 H190170 H62506 AA571805
AA157123 H21637 R40722 AA614207 R53022 AA303826 R62339 AB18429 AA87755 AA543238 AB11321 AA023268 AA276446 AA66995
F19074 AA345370 AB68776 AA503325 SA4881 AA378844 NB5780 AA008985 F29657 W52257 AA131229 AA787007 AA953024 R94845
H28332
15 131011 79701
BE307661 H70180 BE254362 BE469300 AA024546 BE42361 AA000543 AA582924 BE245824 AA024775 AA332373 AA332374 AA330550
AA084266 H68536 AA577890 R83455 AA674699 R20350 BE267908 AA097309 AA33686 AA143370 AA053342 BE257831 AL00222
AA303698 H62374 AA030416 H51368 AA042759 AA038976 AA02693358 W89161 AA336600 AA0567305 F11649 A187160 R65234 R93949
AW250312 AA057745 AA215726 AA450431 BE512806 AA458740 AW894829 BE519049 BE077016 BE548871 AW404030 W21514 T27273
H406197 W3019 T3041 AW952016 T27342 AW091615 AA334727 AA038686 BE690496 BE091495 BE091076 N6356 W52357 N22743
AA538522 AA024582 AA519163 AA027255 AA718044 AA026076 AA148554 DE340385 AA085937 AA536247 AA571805 BE32054 AA5877
AL04121 AA053343 AA591735 AW271278 AD088812 H63512 AE229685 AA421006 AW723565 AW539472 AA054222 AB23745 AW473356
AA453254 W52321 AA256220 AA075525 AA067754 AA619396 BE244907 H48800 AE276992 AA681818 AA465218 AW080876 AA813504
R90914 A124406 AA264339 H69587 H77711 AA674790 AA770572 AD04194 AA435687 AB287762 AW074674 R682346 AW074495 AA4339981
AA77808 AA033952 AE71177 H42212 H60808 W52220 AW72271 H51070 AW261612 DE5682 AE103371 AB91944 AA57345 AB05863
AW52087 AW050297 AW061756 AB81338 AA004971 AA282896 AA025552 AA645434 R461159 BE52679 AW03376 H42250 H41465
BE246448 AA615573 BE513269
101032 106181
BE20854 W55674 H18172 NML000290 BE283720 R8471 J05073 AA191233 AA331034 AA70720 W21456 AD16321 H47465 AA919223 A2302606
AA781116 C04493 NB8030 AA534505 F28198 T28890 AW6607 H015730 F33616 AA335844 AA43296 F24781 AA125673 C32903 F28982
Q0529 F33165 F38087 F22479 A150239 F35636 F34462 F36611 F24672 F23720 AB018136 F33326 AB9189 F25107 F40142 AB00819
AA305561 AA647198 W50414 BE264368 F31524
101042 59211
T46338 BE236864 S82485 T62130 AW12608 AA962194 T57687 AW237678 AA770055 AA671509 AA613961 A1510520 AA005032 R43724 AA538751
AF016492 NML 001073 H00511 J04528 NML 001074 AB281970 AA7406229 AB304148 AW555524 AA333838 AA533838 AD27811 A12145816
AA4816812 AA042250 AB60135 AA091488 AA14235 AA025122 AW001383 AA629336 AA241650 AW201676 F33732 AA159676 AB620317
AW702407 AT02800 AA64530 AA723002 AD09072 AE0115657 AT053988 AA294360 AB572446 AA554579 A735546 AA004482 AT217128
AV55440 H63259 R00611 AA397686 AB60226
131148 520611
AW935375 BE263938 AA561228 AB88629 AW239652 AB115330 AA238464 AA715509 AA613961 A1510520 AA005032 R43724 AA538751
AD27814 AB589431 H4817534 AD023356 AB892256 AB65544 AB69589 A1378581 AA72890 AA073610 AA250334 AA624309 AW002396
AA027050 AA115322 AE125197 AD077573 A1516326 AA435055 AA037735 AA043843 AA464317 AA671805 AA035403 R70208
A1573933 AA110331 A1146463 AB128457 AA363589 AA269597 AB06963 A552817 AW157775 A1092888 AA19413 A1471235 BE541556
A151905 N60505 AW472733 AB858598 AA682254 AW117913 AB82734 AD022434 A151317 AD070597 A1572472 AAB3108 A124841 AA03086
AA46687 AA23195 AA572534 AA580370 A1587086 A0140811 AW424097 AB303700 R25355 AB830390 AW104925 R63720 AB28461
AD279533 A017512 AA32564 A552869 AW147075 AA034098 AA155711 BE348984 AA358584 AA1516761 AA510453 H7790 AAE28308
A157115 H69746 AW72309 AW70612 A389226 N60272 AB098960 AD029377 AA332972 AA051023 AB8374 AB6339 AB11026
AW652621 AA614431 A1679511 AD214444 AA634360 AA159815 AB14528 AB85784 AA050029 AA050026 A1502542 R269131 AA400373
AA833331 AA581814 BE12288 AB025152 R38317 H01942 AW665526 AA081477 AA10774 BE251615 AW10774 BE68424 AA256590
R79494 R22371 BE006080 AA253194 AA064583 W30883 BE136116 BE037311 A291596 AA258741 AA1816219 AB834596 AW236427
BE351407 R237177 R7165 AA45385 AA004657 AA23854 AA060236 AA096932 BE000173 AA025522 R27155 AW795741 A121698
AA295799 R63767 T24990 AA38212 AA328285 BE11673 BE181569 AA084494 R97013 T45456 C00358 AW332769 AA610151 AA074656
AW999031
50 100409 156831
D69597 H18311 AA356702 AA423965 AA672696 AA949846 AA940836 T23880 H03999 R51058 AA029636 H77445 H1602 T84739
A002107 AA057330 H47819 AA001632 BE042952 AA057877 R07807 H49480 AAE32722 AA230338 H45411 AA19297 H57760
AA837329 AA518204 AA619218 H51046 R66077 R241818 R65741 A061305 AA170354 A739572 A42911 A412735 BE24463
AW341005 AW368448 AA067669 AA001633 AB113365 A148448 AW513472 A1512963 AA19243 AA029296 AAT72739 AA462339 AAT770879
AA19051 A513191 A5195281 A1458979 A145081 A1087126 AB304008 AA449294 AAT97338 A1269593 BE042939 R65018 H14 BE254198
AW951818 AD39560 AA253386 AD272907 H78720 AB177947 R24247 H6870 A29047 F2 H4312 A4302198 R65032 A430498 AW771346
A333220 A763797 A554796 AA450309 AA068665 R06688 T03048 A333987 AW022337 H78726 H77451 AA643239 AW119401 H510376
X84713 A559534 A5650317 AD217003 AA026684 AD225211 H51256 R24515 T01129 C052726 AAT133065 P42287 R18005 AA007400
AW161406 R90718 AA328433 AW163311 BE065910 W22101 A2298217 AA163440 AA770117 AA337340 AW044142 AA045950 AA445927
N59157 AW256203 H46577 H18977 AB338930 H47012 AW105475 AW013946 H1387 AAT21201
101170 81131
AA37659 AA532004 A372419 AB004068 BE31257 AA248024 BE22889 AA673387 AA057180 A372421 AAT537913 A514161 A372592
AA177570 H4674 AA376697 F46432 D58544 A007197 A47191 F35330 R25094 AA13351 AB89482 A156442 T51382 AD018320 H45626 T61415
AA331486
131186 81421
BE20074 BE259747 BE410297 AU007544 H68746 AW732306 M26733 BE280182 BE516578 BE27196 BE364496 BE365956 AW723409
AA583335 BE274958 BE276198 BE068068 BE28671 BE304436 AW732808 BE246632 BE410018 BE269603 BE410018 BE269603 BE363966
BE296645 BE290174 BE291930 AA519300 AB31257 AA062624 BE22889 AA673387 AA057180 A372421 AAT537913 A514161 A372592
BE51349 AB369142 AD262161 AW570306 BE365874 BE156397 AA0603394 BE541559 A330493 BE295197 BE407516 AB31549 AW727145
AA564569 BE26141 A2829256 AW731781 AW009966 A166792 AA490719 A1125048 AB99551 AW13495 A538381 AA812401 A608400 A608400
AD03805 AA34469 AB018163 A387367 A17769665 BE127820 A356585 AA113956 A473964 A1946443 AW776976 AA113937 BE453626
AA544601 AA467342 A375129 AW083734 A7068645 BE512846 BE378992 BE413694 AA280409 A141373 BE537647 AAT12628 BE453031
BE36039 BE291123 BE539644 BE480771 BE36985 BE296373 BE267330 BE260146 BE296872 BE28151 BE29464 BE29137 BE30310
100447 132741
NML 011267 BE263826
AA745746 A1387558 AA001463 BE315492 A116960 A232345 AA324913 H4434 A372774 AA159421 A272720 BE301022
AW033961 AA66276 AAE296350 AA129313 H143684 AAE30436 AAE30436 AAE30436 R52667 AA193935 AAE30436 AAE30436
AA37659 AA532004 A372419 AB004068 BE31257 AA062624 BE22889 AA673387 AA057180 A372421 AAT537913 A514161 A372592
R63491 R50032 AA338016 AA325142 AA299317 A515209 AA445457 AA527590 AAE024341 AA380320 AB86803 75981
A0143210 A105469 AB008096 T33661 A22334 T30945 A23096 T33219 H17555 AA477604 AA323721 BE329252 AAE326015 BE240543
AD27722 AA341631 AA11008 BE5864 BE356340 AA006612 R67892 AA083844 AA29683 BE334689 AA04699 AB008181 A3742420
A583017 A1833732 R40882 AAE73744 AAE73744 AAE73744 R68003 AB91469 AA000000 AAE021487 AW011829 A338088 AA37620
AW26585 BE5655 AAE23403 AAE54197 A333326 AAE15454 AAE01257 T03448 AA18846 AAE14571 AAE05398 AAE53739 R53899 AB09208
AD212743 A0740981 AAE291537 T33644 AAE55753 T33610 AAE02498 AAE12707 A3724181 A15022 AA84897 A339970 A178784 A178784 A178784
AW083823 AAE78837 AA5675901 AA40596 A4482198 AAG33514 A887011 T33218 AAE073945 AA872949 AA75040 AAE18669 AA405970
Z3828 T33660 F01690 AA019030 AB868030 BE38861

[illegible]

PCT/US02/17594

WO 02/098358

PTC/US02/17594

			AAT17969 AAT11740 BE54902A BE271002 AA054963 AW169205 AV054316 AW169206 AA062534 AA020310 BE540821 AT260220 AA069920 AT271902 AW169205 AAT17969 AAT11740 BE54902A BE271002 AA054963 AW169205 AV054316 AW169206 AA062534 AA020310 BE540821 AT260220 AA069920
			AA049445 AAT50565 AAT29516 AA1136329 AAT21692 AW166537 AA1100443 AAT22952 AAT21824 AAT07714 AAT10530 BE2707016 BE510295 BE268699 BE397539 T65322 T70457 BE269681 T28038 BE270575 BE500363 BE267605 BE513820 AAT0778843 114577
5	130860	28833_1	BE067133 AAT61214 AA035752 AAT071007 F06002 H06883 H04908 AA386543 BE167181 AA03646E BE163316 W7391 AAT37002A W121265
			AA370375 AA055103
	130693	229704_1	BE0537 AA065942 T97103 AA341163 BE58243 AW1770394 AAT487202 AW096414 AAT23375 D00966 D00411
	123477	40683_1	AF271515 BE018076 AAT470293 AW0593351 AE569865 AIC03643 AW385923 AW005007 AAT769437 AAT19677 AE563835 AA512883 AAT3431295
			AA099331 AIC029339 AAT08767 AA570116 AW061110 AAD43795 BE074895 BE265266
10	108406	113761_1	AAT17524 AAT07525 AAT130690
	115652	54227_1	BE063339 AAT005659 AAT016075 AAT021330 AAT51405 AA0511336 AAT58161 AAT014902 AAT176116 AAT235237 AAT4121401 AAT016167 AAT052594
			AAT01336 AW007065 AA033942 BE044297 AAT016459 AAT143157 AA258266 AA455328 AAT061391 AAT018988 AAT313747 AAT197302 AAT378654
			AA043130 AA01050 AAT060522 AAT77056 AAT02189 AAT6751276 AAT513866 AAT25645 AAT557796 AAT41194 AAT63257 AAT1583423 AAT25761
			AAT55823 AAT038307 AAT05006 AAT578406 AAT051441 AAT31741 AAT013400 AA530322
15	100654	19r_HT2969	AAT3765 AAT0977 A15293 D17029 D17107 D17171 L00132 L00133 M12523 M13075 M13076 M9216 U22961 V00494 V00495 X51363 X51364
	100655	19r_HT2970	X51365
	100793	19r_HT4191	589027
	100231	genbank_AA194776	AA194776
20	102208	6735_9	U22561 AA023523 AA050337 AAT174733 AAT162802 C00092 AA035357 AAT190619 AAT199244 AAT02450 AA002296 AAT378195 AAT029170 A106653
			AAT127795 AAT13846 AAT17389 AAT599465 AA0629390 H43036 AAT01388 BE9894 AAT021196 AAT145413 AAT055022 AAT09426 AAT38273 AAT074570
			AA05096 AAT047466 AAT26040 AAT327614 AA024512 AAT383957 AAT150873 AAT33101 N07005 AAT41254 AAT363191 AAT01237 AAT00709 AAT029400
			W56549 T03036 AAT00127 W00143 AAT063057 AAT37548 AAT59255 AAT567103 W8444 AAT052516 BE03374 AAT129740 AAT129740 A133241
			AE06409 AAT051616 AAT133743 AAT74602 AAT13364 AAT053272 W00494 AAT12523 AAT027526 AAT133120 AAT054802 AAT174993 AAT114729
			AA04516 AAT084116 AAT064959 AAT73681 BE5706 AAT075296 AAT110799 D17107 AAT100047 AAT190165 AAT242416 AAT242416 AAT32942 AAT133684
			AAT133345 AAT1133290 AAT133304 AAT179486 AAT027484 AAT110717 AAT074624 AAT14515 AAT053516 AAT110642 AAT114559 AAT114498 AAT114759
			AAT27588 AAT054960 AAT14753 AAT114666 BE98184 R00011 AAT064697 T65031 AAT207701 T71735 AA363536 AAT35599 T04046 H464599 A133158
			T74675 AA04750 AAT1431 T52939 R50261 T20561 N08352 T51198 T74635 AAT02490 AAT35252 AAT054071 AAT174745 AAT114663 AAT133014
			AAT132999 AAT133100 AAT064825 AAT06479 AAT133663 AA343347 T99031 AAT233983 T3977 AAT44520 T52260 D16981 T40401 T50671 T53826
			T69195 AAT133061 T50850 AAT00677 AAT091136 AAT343608 T64111 Z00079 N5507 T87485 AAT133622 AA343370 T40705 T69617 T5349
			T74620 AAT075316 AAT110018 T40121 T57381 AAT114468 AAT433272 T51362 AAT114589 R00691 AAT10629 AAT063503 AAT140543 AAT343661
			AAT33220 AAT343562 AAT13715 T68549 AAT118480 T5284 T35961 T51400 T71576 T5690 AAT343125 T72126 R04135 T53320 T39972
			T3896 AAT17476 AAT132925 R0027 AAT46458 AAT133690 T03630 T08735 T50930 T70245 AAT44682 T0096 AAT14702 N08011 AAT1305
			R10973 AAT055020 T90625 T50689 D17029 AAT133703 AAT33805 AAT133040 AAT13017 AAT04857 AAT110730 AAT074637 AAT20567 T51700 T32317
			AAT3450 AAT174743 AAT342424 AAT343281 R06652 T64739 T40163 T06628 T81661 T3719 R0482 AA051730 T39931 T35962 T40136
			AA343004 AAT17425 H77374 R00674 AAT065049 T64512 T55916 AAT25733951 AAT005916 T6031 T69176 T73368 T58785 T612301 T39955
			T69512 AAT114876 AAT06716 AAT035710 AAT52753 AAT114795 T83564 AAT341869 T8384 T55599 AAT14710 T51776 AAT34521 AAT114714 T55102
			AAT11009 T82694 AAT14854 AAT308675 AAT343932 T53636 T46969 T64721 T55508 W00241 AAT54918 T57945 T60513 T43634 AAT04000
			W08731 T21851 T46209 BE54053 T73211 AAT114590 T48317 T55965 T74857 R84225 T65022 T62231 T74946 T76976 R02676 T91966
			AAT039974 AAT08471 AAT051457 AAT78102 AAT02062 AAT162792 AAT68421 AAT064737 AAT06517 AAT936993 AAT133117 AAT62224 AAT91548 T83922
			AAT05112 AAT02669 AAT14694 AAT02702 T81475 AAT133526 AAT03251 AAT041769 AAT036354 AAT14720 AAT133526 AAT046980 AAT024042 AAT114536
			AAT490051 AAT242944 AAT07489 AAT060438 AAT133416 AAT07489 AAT060438 AAT133416 AAT07489 AAT060438 AAT133416 AAT07489 AAT060438 AAT133416
			AAT055059 AAT0977 T62990 T71374 T82924 AAT117474 T67411 T68318 AAT064689 T59624 T99010 T58092 T6302 T6322 T2906 AAT01604
			AAT05880 T62896 T69430 T95111 AAT02050 T73300 W52657 T71864 T69118 W52664 AAT114680 T62093 T51797 AAT522363 T73317 T63128 T929581
			T50618 T69118 T53196 T57212 AAT36168 T61612 T69467 T6290 T62912 T72917 T72917 T74886 AAT02448 T57212 T57203 R49461 T711 T73619 T83891
			T69118 T69118 T53196 T57212 AAT36168 T61612 T69467 T6290 T62912 T72917 T72917 T74886 AAT02448 T57212 T57203 R49461 T711 T73619 T83891
			AAT02729 T55539 T90273 T73339 AAT194930 T54846 T71650 T71305 T71287 T53577 T73452 T68562 AAT02936 AAT31290 T87751 AAT174983
			T51579 T51651 H06980 N07374 AA443453 T42466 H06972 N53698 T68447 D11809 D12142 T64300 T28201 T55064
102209	entrez_U32114	U32114	
118475	genbank_N08548	N08548	
132994	45922_1	AA112748 AAT090915 AAT110058 AAT075355 R58494 AAT25984 A25993 T31004 AA043040 AAT360936 AAT366355 W05563 AAT360733 AAT57205	
			AAT309629 AAT516897 AAT372477 H00661 AAT517716 AAT93023 AAT252105 AAT298472 AAT404152 AAT770121 H01681 AAT112137 AAT114348
			AAT250273 AAT143745 AAT067636 AAT041459 AAT150645 AAT620485 N76147 AAT383531 AAT36646 AAT165865 AAT024087 AAT072432 AAT018193
55			AAT130173 AAT090392 AAT11443 AAT51689 AAT069062 H00992 AAT4456 AAT399842 AAT033751 AA050133 R07994 AAT074739 AAT085896
			AAT33709 AAT06755 AAT87281 AAT07651 AAT05412 AAT07489 AAT07489 AAT07489 AAT07489 AAT07489 AAT07489 AAT07489 AAT07489 AAT07489
			AAT48124 AAT151633 AAT200035 AA491168 N6714 AAT06252 T21234
			N58668 AAT155271 AAT030368 N06067
43362_3	AA159901	AA159901	
120226	genbank_AA159901	AA159901	
134921	22921_1	NM_026481 AAT15147 AAT201961 AAT140037 AAT32330 AAT03094 AAT3713 AAT05505 T60712 AAT39925 AAT24055 AAT021385 AAT28720	
			AAT03335 H73580 AAT0554 AAT070883 AAT379135 W09314 AAT152800 AAT407356 AAT5690 AAT56246 AAT03243 AAT39226 AAT31570 AAT391070
			AAT725032 AAT26743 AAT040620 N36044 W36390 AAT39065 AAT39134 AAT347212 W52922 AAT02447 AAT02447 AAT02447 AAT02447 AAT02447 AAT02447
			H43244 AAT3613013 AAT158227 AAT080452 AAT290212 N09026 AAT070629 AAT02862 AAT097 AAT083143 AAT202032 AAT039675 T99652 AAT36191
			AAT17601 T12593 AAT05671 AAT062634 AAT710180 T11392 AAT97692 AAT97529 AAT77266 AAT066176 W31474 W31387 AAT02495 AAT31486
			AAT17594 AAT72403 N3635 AAT09455 Q20495 W7043 AAT14504
120670	genbank_AA20079	AA20079	
129523	18045_3	M13231 X15019 X05776 M9838	
106293	genbank_AA09155	AAT069155	
101405	entrez_U26514	U26514	
131164	24637_1	AAT113607 AAT15696 AAT02432 AAT0902 AAT156960 AAT157922 AAT068164 AAT143603 AAT160636 AAT112426 AAT160458 AAT121056	
			AAT050686 AAT13260 AAT158778 AAT155367 AAT155702 AAT159765 D02138 W52865 AAT159245 Y00603 AAT055024 NM_002276 AAT142005
			AAT128752 AAT01009 AAT07802 AAT051569 AAT158611 AAT161162 AAT190395 AAT050418 AAT06397 AAT723416 AAT294396 AAT12003 AAT040184
			AAT153496 AAT220351 AAT3107 AAT049439 AAT073633 AAT159031 AAT00037 AAT099451 AAT091547 AAT43771 AAT090109 AAT00118 AAT023594
			H20435 AAT327090 AAT29155 T82200 AAT065666 T69562 T611168 H44831 N10517 AAT03693 AAT127516 AAT32113 AAT062944 AAT07479 AAT07479
			AAT382760 M13203 AAT368603 AAT07784 AAT07784 AAT159878 AAT06958 AAT062632 AAT074471 AAT148670 AAT07687 AAT06599 AAT295457
			AAT24021 AAT06576 H26193 H25997 AAT164358 L47725 AAT06283 AAT07024 AAT02263 AAT093619 AAT346319 AAT450315 T71163
			AAT181028 AAT11053 AAT158042 R24917 AAT56362 AAT53551 AAT081015 R70187 AAT2162 AAT119053 AAT11573 AAT35703 AAT0430035
			AAT19089 AAT090855 AAT062293 AAT050124 AAT150916 AAT110689 AAT095445 AAT151978 AAT49447 AAT021437 H02852 AAT0437 AAT375842
			AAT150277 AAT07698 AAT068132 AAT0494 AAT16529 AAT07964 AAT16510 AAT113130 AAT45294 AAT154797 D5817 AAT07490
			AAT064555 NM198281 AAT64309 AAT513787 AAT41361 AAT46163 D59487 D520424 AAT471 AAT115774 T1503 AAT19045 AAT52060
			AAT61487 AAT655127 AAT36596 AAT295862 T84107 T40993 AAT20016 AAT117874 AAT063036 AAT441389 AAT130962 AAT07023 AAT911723
			AAT38432 AAT041902 AAT37806 AAT53767 AAT63492 AAT570319 AAT126294 AAT101016 AAT53915 AAT37910 AAT95768 AAT02606 AAT53315

PCT/US02/17594

1

WO 02/098358

PCT/US02/17594

	313637	2268.9	AK000742 AW593432 AT105785 NMA 016448 AW125743 AK001261 AA364452 W90163 AK001206 AW674785 W90164 BE537327 AW668557 A3360528 AW765212 BE538946 AW730179 AW665799 A2247747 BE532377 AA846697 AA913841 AA505890 AA730175 AA038673 AW60576 A3176959 A0187480 AW59881 AW598644 BE540061 AW576359 AW674003 A3336226 AA5045079 R05900 AW271590 A001801 AA026058 AA080693 AW504533 AA361353 AA561038 AA622192 A3053010 AA69135 AW602881 BE1327000 A290112 BE19678 AA643722 AT338397 A263853 A258992 AA873024 AA840451 AA904417 AA263730 AA835796 H50141 AF080007 H65015 AA050538 A005244 AA535437 AW972174 AW678910 AW70041 AW010293 AA548124 AW676633 AW976986 BE178095 AA628294 AA743595 A021480 AA533000 A021487 A3200691 A0175138 A1732149 H88053 A252206 A21302611 H88264 AA2293979 AA232005 AW676351 AW295400 A3436767 AW1298044 A0559095 A263065 A0262454 AA026451 A3431910 A0261259 AW590242 BE460091 A0205524 A0202663 A0342059 AA0202517 AA846688 AA348814 A227058 AW69095 AW778987 W040485 T35169 AA169459 AA191260 AA136391 AA628791 AW869351 N87347 AA62226 W07100 AW671106 AT792436 AW006313 A1732626 AW302105 AW704054 AW096409 AW068298 AW268789 BE138591 A349541 BE049152 A336511 A336490 A336599 AW32938 BE139030 A3349711 AW300344 A252136 A454022 A144108 A252466 A0733716 A349804 AW501920 A251159 A3111053 AW271910 BE138422 BE138405 A253962 A028961 AW002617 A345087 A0251185 A0251336 BE113804 AW09773 A2527261 A1252896 BE138557 AW099115 A1252823 A035714 AW0301523 A0353755 A055556 A054200 A035780 A035446 A054006 A053514 A035446 A035940 A1140633 AA613834 BE138636 AW302036 AW271147 A3456440 A1513914 AW379055 AW272051 AW272051 AW271022 AT141536 AA594304 A3307973 A1448950 A471936 AA478296 AA148951 A0519327 AA510677 AA732008 N25957 H95949 AW975445 A027844 AW07785 BE50656 AW205418 A0385859 AA033210 D06275 D08060 D06300 D5841 D06620 R95972 A1502456 AW668820 AW913981 AW818676 AW161004 AW618895 AW609933 AW392990 AW582601 A1502456 A818225 A818124 A17905 R09750 A054569 A335395 AW652071 AW917261 AW015807 A0551144 AW538095 A1735759 AA304513 A1188319 AW671654 A0169853 A1769145 A0272367 A021055 A871580 A016117 H56077 BE116622 BE162152 A242745 W58441 W58427 C04963 N54290 N54238 A0767362 N51558 A4587542 BE173119 W03745 W03727 W784523 A009636 AW975392 N74169 AW816906 AW87602 AW265836 A140754 AW188619 A4587542 AW03722 A014812 AA808213 N50636 W02972 A014731 AA8263043 AW191931 AA516924 A4741240 A000665 A014777 A1358045 R75338 AW340779 A0065334 A0182186 AAT45276 A1478333 AW187989 A911151 A002208 AA176892 AW057790 A290209 A036705 R05657 AF147590 R05659 AW252176 AA604126 AW058157 AA604799 A020551 A0037933 A3358915 A1743933 A337949 AW454268 A2527321 A1 A046020 AW673743 A2426235 A0931376 AA604921 A1 BE26566 AW073887 AW083504 AW089401 A1978793 BE16989 A2537745 AW599403 AW64381 A557398 AW392189 AA535583 A067545 A090698 A090600 A090048 AA516526 A012053 AW151024 A1027866 A0921563 AW511653 A011596 A0996818 AA338664 AA337039 AW095212 AA336549 AW064722 AA506487 AA37383 A0688616 BE550194 AW994408 AW996239 A9139705 A1723883 BE545311 F13555 165504 AW245035 H95618 BE253221 A122073 BE39462 A067259 AW15154 A074244 A1309648 AW518932 A148420 A333800 AA47496 A025124 A1713770 A143549 A048037 A071458 BE2532 A0514498 A3339729 A538226 A9151161 AW152296 A1495657 A031330 AW000645 AA471017 D59282 AA592190 AA58195 A091127 BE251450 WA7525 AA134047 BE391212 AA230333 AA376395 A0304871 BE167342 H87402 AA531722 WA5754 AA715557 A025438 A080489 A0241617 AW138007 A835345 A1134048 AW74874 A822227 A814987 A093395 A022886 A0501467 A022506 AW06386 C03914 A146960 AW257919 A0117302 N53216 A1967301 AA251715 A19695877 AA726898 AA76540 AA743170 A1133990 A1128582 A0129770 AW072506 A0505700 T78413 A0128933 A043067 AW080038 AA694545 H01994 A4730423 AW576123 A475644 AA98781 A1048528 R19187 A1339591 A1338964 T86956 A036097 BE349489 A080004 H02001 R26552 AA573927 AA464893 R24078 W58759 A1189805 AA844323 A089162 A09173161 A0817045 A0243803 T24484 H68847 A264825 A0455017 A07751676 A069576 A279716 A440451 A5250234 A068541 A1125533 A112521 H77025 H68807 A094295 A087017 AW071336 T87876 Z80753 R24182 A173036 H69590 BE17747 A0554372 A49381 A48616 T85132 R11436 BE1612 AW385362 T03032 AA458281 A0876696 T34568 AW67362 AW036892 A470245 A287676 AA641833 A085015 A19782619 A070243 A0740854 AA700865 A022697 AA650814 AA654815 A815704 A07339 A0030231 A022776 AA051659 AW0635947 H24255 AA626395 AA393273 A1515381 A095987 AW051657 A140525 AW650272 A3382139 A125648 AW296134 AA622260 T68640 A337943 A354941 AW511303 BE014493 A4211027 A087903 A0952430 A063871 BE349647 A0167164 AA947662 A371477 A014566 A0001478 A3319342 A0471530 A119130 R13701 A3363659 AW959490 AA06905 AA65101400 F07067 Z42134 AW238014 AA134238 H15216 R19551 AA359561 A19695786 Z43960 AA448444 AA133248 R0902 A0041707 WE2631 BE35394 AA404489 BE490081 B71262 H65897 R02836 R77316 R07005 N79564 A150154 A0427218 H45210 A052632 A020276 A1153362 A01752221 A0834549 A477775 A131308 A0400189 A020268 BE176956 A0042927 AA054432 A020354 A1450594 N55659 AA459974 A0677030 A0677030 H15166 N55021 N59699 A331978 A05156 A0282642 R09517 A067486 N59661 A115893 A373105 A421080 A342277 A0291327 A0291327 A024801 A0243833 A13032479 A13595914 AW304855 A1374393 AA700701 A1778715 AW500261 H09112 A3523791 BE328612 R72787 A065130 A1824048 H65802 A094930 AW645490 AW197384 A114027 A554805 A0116932 A01805 A068887 BE30661 D80402 AW075296 A060747 A000334 A0242750 AW594340 A0471090 R93133 R01671 R37785 AA878222 R02657 AW279212 A052296 AW014397 AA531096 R33536 N69316 R37527 R50560 R51008 AW512986 116256 117085 A0091075 A00966 A151111 A077810 AA613265 AA13434 A2923417 A0703130 BE047711 AW653038 AA156485 BE152441 AA263351 W39493 A21877 R67724 A095652 AW68795 R38340 A084947 A0939564 AW157184 A151184 A291458 A0939564 AW265158 W06397 BE173171 A151153 A077004 AW58007 AW68887 BE30661 D80402 AW075296 A060747 A000334 A0242750 AW594340 A0471090 R93133 A242003 A4249641 A0256328 A035016 A6387191 AA195667 A027533 A3151840 AA417241 A0436735 A0954661 A215929 BE467827 A000996 A194726 W78671 AA048900 A088860 BE327986 AW150774 A527287 R095620 A001246 A016216 H69844 AW020195 A290564 A035484 A052846 A422673 A0179863 AW02938 H69844 A0808255 A0544398 A120111 A091116 A2942529 A263951 A013595 A193362 A411202 AA403844 AW539194 A1744662 A169110 A1359376 A053555 AA643155 Z38179 T24811 T98139 A073735 A9378066 AA548906 A3351272 AW075222 A0260901 A215628 A0531650 A04522952 AA512893 AW66597 A0781491 A0973048 A0110053 A034606 AW192528 AA227395 BE327414
--	--------	--------	---

WO 02/098358

PCT/US02/17594

14943	29197_1	Y002721 H# 1706 X06300 A7098939 A3366724 BE14149 BE613019 A481617 A1460416 A4852829 A4006392 A2026251 A4278384 A3430903 A4961259 A4279928 A3308970 BE082133 BE620696 BE620344 AF154322 AE083775 BE045119 A809169 A333226 A5089947 A6879147 A0051286 A4676781 A6119661 A463969 A4725015 A467796 A4719320 A464041 A459874 A481659 A498610 A428189 A5176894 A4734302 A566748 A4678755 A4888424 A4970204 A4847613 A4053880 A4356816 A3377603 A4314704 A4313715 BE26254 A4213845 A4617610 A426982 A491353 A559883 A4939377 A4261869 A4971664 A4276912 A4506336 A532362 A423556 A4315900 A485531 A474770 A4371043 A425742 A4635876 A4806100 A4282829 A459060 A4357771 A4337408 A4781575 A06162 BE527294 A4281741 A037114 A481551 A4748439 A406221 A4829563 A4278152 A4002602 BE625966 A492210 A4605596 RS7512 W79066
14946	338282_1	A0077229 A4242329 A4242439 A4932668 A4919074 A40001485 A4515371
14947	238473_1	A433527 A426541 A4677233
14948	432790_1	A0029114 A455588 A4911938 A0693875 A4926984 A4744306 A4744331 A447443 A4744022 A49873026 A453081 A4932621 A501168 A880221
15	323410	A0119883 A4203954 H30912 A4135542 A650131 A40021767 D62063
15	300551	A4948900 A4247736 BE673504 BE334636 BE336379 A4840756 BE636238 A4330655 BE472697 BE262630 A116248 RS6369 BE818109
15		R07665 A4642543 R48262 A4287784 W22131 W6837742 A00577742 A00512315 BE240157 A4775101 A4282632 A4903694 A4273221 A0050537 A0665290 A0673294 A4739152 A0007712 A3320016 A1022382 A5771183 A4563628 A4953840 A474213 A4245761 W68308 A893544 A433056 A48494 A4812666 A4639677 T06935 R87857 A852610 N8328 A4924790 Z T0692 A428828 A405665 BE6294545
20	300566	A4571688 A4700328 A40534 181
20	316244	R44526 A421651 BE454329 H6709 A894036 A803494 BE241794
20	228226	A4640781 A0518716 A4348566 A694445
20	156168	A807883 A40025512 A4806939 A4857895 A4145093 A4723744 A4334050 A481046 A4204307 A4935072 A4836440 A49582751 A287341 A451357 A671456 A48674317 A4157639 A4923349 A330603 A49166139 A817052 A4148795 A4045636 A3306119 A4627270 A4513998 A8978953 A4072242 A491563 A4933089 A741454
25	322539	A4913308 A4744532 A4677631 A805964 A4623675 N6840
25	256807_1	A4178955 A4957033 A049645
25	316943	A1284219 A4661616 A631144 A4023594 A4897028 A4190512
25	322569	A4301270 A4301379 A4301396
25	322579	A4151687 A402942 A4110549
30	316720	A4292266 A49733560 A4760698 A0074092 BE664545 A0073677 A5514801 A0073701 A4717020 A523738 A4580870 A523976 A493326 A070229 A4563914 A4582842 A5171457 A4937634 A8806614 A439423 A49291875 A4551874 A8182314 A492227 A4397375
30	317572	A4615373 A378428 A570316 A4135126
30	300702	A4075481 A4075490 A4075087
30	322620	A4305927 A4776470 A029656 A660377 A890467
30	323645	A4945014 A4902240 A860713 A4310868
35	316465	A4954774 A4954775 BE350883 A4349525 A1144210 A4764736 A4774177 A4871426 A4337556 A4811497
35	308616	A0000142 A40243187 A0735953 A4906395 BE005029
35	315841	A4158397 A119461 A4679304
35	316843	A4979430 A4288325 A49365349 A4917912 A49179160 A49179165 A49179167 A49179168 A49179169 A4917916A A4917916B
40	300627	BE452706 A4228425 A4228535 H80602 R83651 H10596 BE432365 A45547391 A4631694
40	324302	A49127711 A4543008 A4002052 A8972328 A060044 H91135 A240797 A4303682 A4871992 A4645937
40	324330	A4684766 A4074221 A4532975 A4474312
40	323763	A000161 A4737102 A050668 A4713501 A1339018 A4107100 A407603
40	315901	A1521538 A4282964 A4026578 A571259 A49296746 T70009 A829914 A4561010 A4879955 A466354 A4908992 A861482 A4290111 A411805 A4523846 A4008328 A4823667 A890645 A4620053 A516110 A40652326 A1978687 A435290 BE262672
45	315936	A4905807 A469094 A4610301
45	302123	A413452 A497620 A4219882 A4751070 A44119924 A4014224 A44552796 W39181 A4119045 A4814358 A4949884 A439330 A758638 W5233 A4932286 A8218581
50	302124	A4678403 A4609167 A4287064 BE003999 A4217765 A49452295 A1848575 A4486282 A0001385 BE635238 BE200936 BE00090 BE000683 BE00066 BE001093 A1138357 A4748694 A474478 A49368265 A53682273 A9134050 A4979762 A4228412 A432900 A4005782
50	317222	A4894880 A4762321 A514673 A751221 A680137 A402510
50	317224	X70080 N42 A04598 A422112 A409205 A472286 A4918623 A4040054 A4023645 A4022807 A4629818 A4541349 A4719218 R68666 H51589 H06666 L2321 A4236371 M61505 A0056213 R6807 D66209 T39129 A4325783 A074652 A081156 A252344 A490001 T19996 H08670 A4948685 A4019478 A4142950 H50527 A082187 D66119 D66136 A4332648 R1193 R11939 A4984947 A4936263 A1230466 A491446 A4984919 R11736 A4984919 H161425221 A4786 T00912 T06966 T36522 A4046577 T06851 A4926952 Z00311 T00767 F1182 A490442 A430326 BE154523 A452087 A4904186 A4904187 A4904189 A4904190 A4904201 A4904202 A4904203 A4904204 A4904205 A4904206 A4904207 A4904208 A4904209 A4904210 A4904211 A4904212 A4904213 A4904214 A4904215 A4904216 A4904217 A4904218 A4904219 A4904220 A4904221 A4904222 A4904223 A4904224 A4904225 A4904226 A4904227 A4904228 A4904229 A4904230 A4904231 A4904232 A4904233 A4904234 A4904235 A4904236 A4904237 A4904238 A4904239 A4904240 A4904241 A4904242 A4904243 A4904244 A4904245 A4904246 A4904247 A4904248 A4904249 A4904250 A4904251 A4904252 A4904253 A4904254 A4904255 A4904256 A4904257 A4904258 A4904259 A4904260 A4904261 A4904262 A4904263 A4904264 A4904265 A4904266 A4904267 A4904268 A4904269 A4904270 A4904271 A4904272 A4904273 A4904274 A4904275 A4904276 A4904277 A4904278 A4904279 A4904280 A4904281 A4904282 A4904283 A4904284 A4904285 A4904286 A4904287 A4904288 A4904289 A4904290 A4904291 A4904292 A4904293 A4904294 A4904295 A4904296 A4904297 A4904298 A4904299 A4904300 A4904301 A4904302 A4904303 A4904304 A4904305 A4904306 A4904307 A4904308 A4904309 A4904310 A4904311 A4904312 A4904313 A4904314 A4904315 A4904316 A4904317 A4904318 A4904319 A4904320 A4904321 A4904322 A4904323 A4904324 A4904325 A4904326 A4904327 A4904328 A4904329 A4904330 A4904331 A4904332 A4904333 A4904334 A4904335 A4904336 A4904337 A4904338 A4904339 A4904340 A4904341 A4904342 A4904343 A4904344 A4904345 A4904346 A4904347 A4904348 A4904349 A4904350 A4904351 A4904352 A4904353 A4904354 A4904355 A4904356 A4904357 A4904358 A4904359 A4904360 A4904361 A4904362 A4904363 A4904364 A4904365 A4904366 A4904367 A4904368 A4904369 A4904370 A4904371 A4904372 A4904373 A4904374 A4904375 A4904376 A4904377 A4904378 A4904379 A4904380 A4904381 A4904382 A4904383 A4904384 A4904385 A4904386 A4904387 A4904388 A4904389 A4904390 A4904391 A4904392 A4904393 A4904394 A4904395 A4904396 A4904397 A4904398 A4904399 A4904400 A4904401 A4904402 A4904403 A4904404 A4904405 A4904406 A4904407 A4904408 A4904409 A4904410 A4904411 A4904412 A4904413 A4904414 A4904415 A4904416 A4904417 A4904418 A4904419 A4904420 A4904421 A4904422 A4904423 A4904424 A4904425 A4904426 A4904427 A4904428 A4904429 A4904430 A4904431 A4904432 A4904433 A4904434 A4904435 A4904436 A4904437 A4904438 A4904439 A4904440 A4904441 A4904442 A4904443 A4904444 A4904445 A4904446 A4904447 A4904448 A4904449 A4904450 A4904451 A4904452 A4904453 A4904454 A4904455 A4904456 A4904457 A4904458 A4904459 A4904460 A4904461 A4904462 A4904463 A4904464 A4904465 A4904466 A4904467 A4904468 A4904469 A4904470 A4904471 A4904472 A4904473 A4904474 A4904475 A4904476 A4904477 A4904478 A4904479 A4904480 A4904481 A4904482 A4904483 A4904484 A4904485 A4904486 A4904487 A4904488 A4904489 A4904490 A4904491 A4904492 A4904493 A4904494 A4904495 A4904496 A4904497 A4904498 A4904499 A4904500 A4904501 A4904502 A4904503 A4904504 A4904505 A4904506 A4904507 A4904508 A4904509 A4904510 A4904511 A4904512 A4904513 A4904514 A4904515 A4904516 A4904517 A4904518 A4904519 A4904520 A4904521 A4904522 A4904523 A4904524 A4904525 A4904526 A4904527 A4904528 A4904529 A4904530 A4904531 A4904532 A4904533 A4904534 A4904535 A4904536 A4904537 A4904538 A4904539 A4904540 A4904541 A4904542 A4904543 A4904544 A4904545 A4904546 A4904547 A4904548 A4904549 A4904550 A4904551 A4904552 A4904553 A4904554 A4904555 A4904556 A4904557 A4904558 A4904559 A4904560 A4904561 A4904562 A4904563 A4904564 A4904565 A4904566 A4904567 A4904568 A4904569 A4904570 A4904571 A4904572 A4904573 A4904574 A4904575 A4904576 A4904577 A4904578 A4904579 A4904580 A4904581 A4904582 A4904583 A4904584 A4904585 A4904586 A4904587 A4904588 A4904589 A4904590 A4904591 A4904592 A4904593 A4904594 A4904595 A4904596 A4904597 A4904598 A4904599 A4904600 A4904601 A4904602 A4904603 A4904604 A4904605 A4904606 A4904607 A4904608 A4904609 A4904610 A4904611 A4904612 A4904613 A4904614 A4904615 A4904616 A4904617 A4904618 A4904619 A4904620 A4904621 A4904622 A4904623 A4904624 A4904625 A4904626 A4904627 A4904628 A4904629 A4904630 A4904631 A4904632 A4904633 A4904634 A4904635 A4904636 A4904637 A4904638 A4904639 A4904640 A4904641 A4904642 A4904643 A4904644 A4904645 A4904646 A4904647 A4904648 A4904649 A4904650 A4904651 A4904652 A4904653 A4904654 A4904655 A4904656 A4904657 A4904658 A4904659 A4904660 A4904661 A4904662 A4904663 A4904664 A4904665 A4904666 A4904667 A4904668 A4904669 A4904670 A4904671 A4904672 A4904673 A4904674 A4904675 A4904676 A4904677 A4904678 A4904679 A4904680 A4904681 A4904682 A4904683 A4904684 A4904685 A4904686 A4904687 A4904688 A4904689 A4904690 A4904691 A4904692 A4904693 A4904694 A4904695 A4904696 A4904697 A4904698 A4904699 A4904700 A4904701 A4904702 A4904703 A4904704 A4904705 A4904706 A4904707 A4904708 A4904709 A4904710 A4904711 A4904712 A4904713 A4904714 A4904715 A4904716 A4904717 A4904718 A4904719 A4904720 A4904721 A4904722 A4904723 A4904724 A4904725 A4904726 A4904727 A4904728 A4904729 A4904730 A4904731 A4904732 A4904733 A4904734 A4904735 A4904736 A4904737 A4904738 A4904739 A4904740 A4904741 A4904742 A4904743 A4904744 A4904745 A4904746 A4904747 A4904748 A4904749 A4904750 A4904751 A4904752 A4904753 A4904754 A4904755 A4904756 A4904757 A4904758 A4904759 A4904760 A4904761 A4904762 A4904763 A4904764 A4904765 A4904766 A4904767 A4904768 A4904769 A4904770 A4904771 A4904772 A4904773 A4904774 A4904775 A4904776 A4904777 A4904778 A4904779 A4904780 A4904781 A4904782 A4904783 A4904784 A4904785 A4904786 A4904787 A4904788 A4904789 A4904790 A4904791 A4904792 A4904793 A4904794 A4904795 A4904796 A4904797 A4904798 A4904799 A4904800 A4904801 A4904802 A4904803 A4904804 A4904805 A4904806 A4904807 A4904808 A4904809 A4904810 A4904811 A4904812 A4904813 A4904814 A4904815 A4904816 A4904817 A4904818 A4904819 A4904820 A4904821 A4904822 A4904823 A4904824 A4904825 A4904826 A4904827 A4904828 A4904829 A4904830 A4904831 A4904832 A4904833 A4904834 A4904835 A4904836 A4904837 A4904838 A4904839 A4904840 A4904841 A4904842 A4904843 A4904844 A4904845 A4904846 A4904847 A4904848 A4904849 A4904850 A4904851 A4904852 A4904853 A4904854 A4904855 A4904856 A4904857 A4904858 A4904859 A4904860 A4904861 A4904862 A4904863 A4904864 A4904865 A4904866 A4904867 A4904868 A4904869 A4904870 A4904871 A4904872 A4904873 A4904874 A4904875 A4904876 A4904877 A4904878 A4904879 A4904880 A4904881 A4904882 A4904883 A4904884 A4904885 A4904886 A4904887 A4904888 A4904889 A4904890 A4904891 A4904892 A4904893 A4904894 A4904895 A4904896 A4904897 A4904898 A4904899 A4904900 A4904901 A4904902 A4904903 A4904904 A4904905 A4904906 A4904907 A4904908 A4904909 A4904910 A4904911 A4904912 A4904913 A4904914 A4904915 A4904916 A4904917 A4904918 A4904919 A4904920 A4904921 A4904922 A4904923 A4904924 A4904925 A4904926 A4904927 A4904928 A4904929 A4904930 A4904931 A4904932 A4904933 A4904934 A4904935 A4904936 A4904937 A4904938 A4904939 A4904940 A4904941 A4904942 A4904943 A4904944 A4904945 A4904946 A4904947 A4904948 A4904949 A4904950 A4904951 A4904952 A4904953 A4904954 A4904955 A4904956 A4904957 A4904958 A4904959 A4904960 A4904961 A4904962 A4904963 A4904964 A4904965 A4904966 A4904967 A4904968 A4904969 A4904970 A4904971 A4904972 A4904973 A4904974 A4904975 A4904976 A4904977 A4904978 A4904979 A4904980 A4904981 A4904982 A4904983 A4904984 A4904985 A4904986 A4904987 A4904988 A4904989 A4904990 A4904991 A4904992 A4904993 A4904994 A4904995 A4904996 A4904997 A4904998 A4904999 A4905000 A4905001 A4905002 A4905003 A4905004 A4905005 A4905006 A4905007 A4905008 A4905009 A4905010 A4905011 A4905012 A4905013 A4905014 A4905015 A4905016 A4905017 A4905018 A4905019 A4905020 A4905021 A4905022 A4905023 A4905024 A4905025 A4905026 A4905027 A4905028 A4905029 A4905030 A4905031 A4905032 A4905033 A4905034 A4905035 A4905036 A4905037 A4905038 A4905039 A4905040 A4905041 A4905042 A4905043 A4905044 A4905045 A4905046 A4905047 A4905048 A4905049 A4905050 A4905051 A4905052 A4905053 A4905054 A4905055 A4905056 A4905057 A4905058 A4905059 A4905060 A4905061 A4905062 A4905063 A4905064 A4905065 A4905066 A4905067 A4905068 A4905069 A4905070 A4905071 A4905072 A4905073 A4905074 A4905075 A4905076 A4905077 A4905078 A4905079 A4905080 A4905081 A4905082 A4905083 A4905084 A4905085 A4905086 A4905087 A4905088 A4905089 A4905090 A4905091 A4905092 A4905093 A4905094 A4905095 A4905096 A4905097 A4905098 A4905099 A4905100 A4905101 A4905102 A4905103 A4905104 A4905105 A4905106 A4905107 A4905108 A4905109 A4905110 A4905111 A4905112 A4905113 A4905114 A4905115 A4905116 A4905117 A4905118 A4905119 A4905120 A4905121 A4905122 A4905123 A4905124 A4905125 A4905126 A4905127 A4905128 A4905129 A4905130 A4905131 A4905132 A4905133 A4905134 A4905135 A4905136 A4905137 A4905138 A4905139 A4905140 A4905141 A4905142 A4905143 A4905144 A4905145 A4905146 A4905147 A4

PCT/US02/17594

15

PCT/US02/17594

1

WO 02/098358

PCT/US02/15954

5	311422	270835_1	F03677 AW636896 AW981342 AA363426 AW966402 BE180950 AW941639 AW242125 AA806114 BE301606 A249498 BE219291 AW506165 A2748487 AW122101 ZB5335
	311465	857586_1	A1758890 A1758865 AW020810
	303954	64568_1	BE246743 AA438942 AW024714 AW242177 AA975476 AW085185 RW536 RW3402 AW545429 T54442 A1399988 RS0073 R46743 A1769699 AW83005 AA317808 AW678000 AW189963 AW986207 AW617123 R73463 AA338104 AB90181 AA485267 AW54604 H219641 T26141 AA458769 RS0074 A1703255 A271945 A224499 AA535828 A621061 A1751546 AB19161 AW766962 A2267290 AB8691 A11 AW560075 AA355590 AA335572 AA422727 AW72752 AW030040 AW53667 AW552562 AW196164 R46744
	310894	740029_1	AA14684 AW177655 AH434594 AM275363
	312105	413662_1	T81819 AW363705 AA703541 AA9370185
10	312108	222153_1	T82351 AA973625 BE7352 AA9537117 A761465 AA290860 AW075000 A1127126 AW293000 A293354
	312197	200163_1	AW05343 T8121
	311587	16193_2	AB28254 AW193082 AW102765 AW035668
	311598	903700_1	AW023595 AW125233 BE350312 BE65094
	310955	715902_1	AA176732 A1550210 BE149569 AW119381 A1898975 AW197294
15	319408	301280_1	AA44680 RW1672
	301582	9344_1	AF034796 NML05625 A0002917 A3255780 N65544 H09394
	318814	1702210_1	WC1381 R36746 Z42619 R19489 R18600
	320099	21462_1	AW411307 AA386114 AF081535 AJ232726 T31599 AF0530074 NML003004 T34235 AF026936 AA353437 AW674908 AA336980 BE265146 AW553589 BE067589 BE067489 AW359666 AW053694 AW063720 AW961615 A7803047 AW674282 A780943 AA470904 AW589431 AW561602 AW133992 A220589 A4574629 AB468334 AA654267 A171417 H56633 AB952232 AB24044 AW176966 AB183950 AA973202 AA432014 H55954 AA68793 BE250534 BE262473
	312226	220393_1	AA315703 T96053 A1796815 A049575
25	312240	576454_1	R36475 R26626 A006320 T87600 R57616 H01236 R79817 R67517 R32555
	312292	68565_1	AW54103 AW46193 H1933 A282650 A283763
	303620	27494_1	AD307358 AW69417 BE116022 BE207157 A205125 BE003963 AW965680 AA34946 AA361821 AA102568 BE146222 D31580 AQ001190 R45887 A1327674 A755276 BE168407 AW040238 AA160646 A0020221 T15658 AA161281 AA143486 A1372673 D08001 A1870013 A166900 AA1155252 A9712026 AW071873 AA139111 AH33765 AW139206 A1376927 A036534 AA678331 AA116066 A1365122 AA1786304 AA150270 AW995939 T86883 AA349465 AA330331 D68000 AA153936 AA364848 A3342621 A1334683 AA351620 AA301787 AW175382 A926390 AA1702362 A4376195 AW04962 AA365373 AA102488 AA109046 A3325211 AA425180 BE326166 H6342 A367726 N94717 A43597160 W8303 AW029967 A9750041 A1021416 AW589616 AA313505 AW951923 AW082735 AW185962 A6567485 A9502580 A464145 A442826 AW062999 A4043406 AA043409 A1353488 AYW104306 A4877117 AA1762807 AA181583 AYW26406 H63454 A9262015 W88955 A1100217 A1735859 A351483 N77642 W52251 A1369937 H11435 AA156066 AA102489 AW139966 AW93453 BE135052 A537668 AW075493 AA654017 A1054330 AA546988 AB00221 A186161 A157009 A0404500 A431107 AW770217 AW1471322 W85009 A1134671 A13471 A1342199 AW126581 A4407690 AA736918 AA748235 AA905001 R31406 AW117332 AA922276 AA370320 AA225176 AW976198 RW17334 R43707 AA780136 A061417 A1620657 A674282 AW974521 AA651778
35	312313	421652_1	A1523875 A57562 R45781
	312361	364252_1	AA523875 A57562 R45781
	312406	765247_1	AA523875 A57562 R45781
	313070	734749_1	AA523875 A57562 R45781
	313077	620465_1	AA523875 A57562 R45781
40	313168	177700_1	AA021098 AA910047 N66834
	313179	513655_1	AA527670 A076101 N66361 AW156229
	313198	261800_1	T82126 AA367503 AW953611 AW054766
	313608	7069_3	T83693 AA529160 A4221130 A422736 AA430375
	321023	363496_1	AW624316 AA577516 AW075980 A672654 A6713755 A964320 A1380443 A4884643 A1358362 AW56570 A2470173 H25135
45	321024	125702_1	AW242219 BE245257 BE247413 A264325 A809116 A1156454 A1199757 A369602 AW136723 A5536875 A176666 A500226 A159726 AA994567 A1326961 A1560412 AW614026 A270184 AA331957
	315687	200730_1	H4674 A1026737 BE053576 AW613553 H6151 A1568625 T76946 AW0526 N62680
	316260	85181_1	AW970605 H5004 AA015336 H66102 AA165342
	313280	229754_1	AW960454 A1265537 U51706 AA740064 AA702720 AA327833
	312689	843717_1	AW450461 A1720165 R185744 D81222
50	319926	37979_2	BE207119 A273515 AW616867 A263784 A3051926 R40666
	320514	25769_1	A150015 AW155237 A431204 AA748122 AA34580 AA741126 AA946605 AA825481 A1807650 A419758 AA460487 AW065591 A9114425 AA931308 T73578 A244696 N48346 A897928 AW976264 AW263086 A654504 AW593142 RS7253 AA393730 AW336771 AW182026 AW895231
	312820	412652_1	A248774 T73584 H07813 A4702493
	312803	434367_1	A4777334 A1069592 H71042
	320663	234846_1	AA334511 AW625606 BE255237 A1792758 R50291
60	313475	83840_1	AA010200 AA926774 AW0316970 A4263372 A3731245
	320697	341050_1	NE2397 N53008 N63029 N63016 N63034 N63876 R62588 AA525236
	312821	410071_1	AA69325 A1027465 H71866
	321326	26266_1	A1033100 AA347036 BE263225 AW961668 A1047207 AA347037 A1076694 A4601010 A5569597 AW139033 AW274622 A1172884 AW895070 AA804340 AWT798925
	314146	183043_1	A5272327 AN294349 A682262 A306704 AA460226 A5115460 A930404 A9080484 A533689 AA236344 A1016781
65	314171	186022_1	BE212655 A12007 A4603610 A4651659 A4243667 AYW182132 AA24046 A1321442 A182694 AA240456 A452871
	313552	116315_1	A689208 AW022092 AA502956 A00116071 AW0115966 A6820231 AWM02192 AA130685 A671862 AWM007997 R65785 AA533163 T65272 H46901 AAW016963 AW172664 A687967 A947380 T57529 AA629377 AW467155 A1789796 A5374598 R08750 BE217182 R63373 A1536969 AA169871 A560026 AA169366 A4944112 AA463623 AYW166999 A8267576 R09174 A434652 A983041 T67439 H06517 R91140 H63522 H62316
	320771	210125_1	R01441 NML0546 R63800 A973036 A1961774 BE237552 AB007726 AWT70041 A13265537 A2118667 A492386 A2411532 AA3011750 A209012 AA486826 R07609 AW682776
	320779	74700_2	AA815354 AAW52696 AW972288 A1597675 BE830067
	320787	500769_1	AW068363 R78323 A1562638 AA090302
75	312939	264696_1	AA499530 A170690 H67631 AA330358 BE166712
	320885	c.k.16	
	339662	CH22_4138FG_41_1	
	336884	CH22_4167FG_46_1	
	336721	CH22_4244FG_83_17	
80	330308	CH22_5535FG_LINK_EMAC00	
	306999	A1138628	
	338316	CH22_8944FG_LINK_EMAC00	
	338561	CH22_7294FG_LINK_EMAC00	
	338592	CH22_7295FG_LINK_EMAC00	

WO 02/098338

PCT/US02/17594

333124 CH22_363FG_81_8_LINK_EM_A
 333135 CH22_364FG_83_11_LINK_EM_A
 333137 CH22_369FG_83_13_LINK_EM_A
 333138 CH22_367FG_83_15_LINK_EM_A
 333139 CH22_369FG_83_16_LINK_EM_A
 333187 43717_1 AA115952 AA078794
 328213 c17_hs
 333516 CH22_772FG_173_1_LINK_EM_A
 333817 CH22_773FG_173_2_LINK_EM_A
 333743 CH22_1009FG_254_1_LINK_EM_A
 333795 CH22_1053FG_275_1_LINK_EM_A
 333796 CH22_1065FG_275_3_LINK_EM_A
 335044 CH22_2357FG_430_1_LINK_EM_A
 333808 CH22_1077FG_279_2_LINK_EM_A
 333809 CH22_1078FG_290_2_LINK_EM_A
 333845 CH22_1114FG_290_3_LINK_EM_A
 333849 CH22_1118FG_290_8_LINK_EM_A
 335149 CH22_2484FG_499_5_LINK_EM_A
 335095 AA642864
 335289 CH22_2631FG_527_2_LINK_EM_A
 335290 CH22_2632FG_527_3_LINK_EM_A
 335293 CH22_2635FG_527_6_LINK_EM_A
 328816 c20_hs
 330961 AA175081
 330532 AA670052
 328164 c_5_hs
 330503 AA759177
 335682 CH22_3043FG_595_2_LINK_EM_A
 330612 AA752347
 336763 CH22_3120FG_604_2_LINK_EM_A
 336765 CH22_3122FG_604_4_LINK_EM_A
 336766 CH22_3123FG_604_5_LINK_EM_A
 336809 CH22_3181FG_617_6_LINK_EM_A
 336910 CH22_3182FG_617_7_LINK_EM_A
 336924 CH22_3197FG_619_11_LINK_E
 328648 c_7_hs
 337182 CH22_3204FG_570_2_
 307111 AI174523
 330032 c16_p2
 330033 c16_p2
 337603 CH22_6095FG_LINK_C20H12
 337674 CH22_6006FG_LINK_EMAC00
 337675 CH22_6006FG_LINK_EMAC00
 337765 CH22_6105FG_LINK_EMAC00
 338186 CH22_6120FG_LINK_DA59H18
 305390 AW080185
 305675 AW168096
 332792 CH22_8FG_3_2_LINK_C461.GE
 334101 CH22_1379FG_327_56_LINK_E
 334049 768165
 334221 CH22_1904FG_360_1_LINK_EM_A
 334222 CH22_1905FG_360_3_LINK_EM_A
 334282 CH22_1671FG_369_12_LINK_E
 302910 386182_1 W77975 W03184
 325859 c16_hs
 327110 c21_hs
 304263 AA062637
 304275 AA070505
 304309 AA112147
 334502 CH22_1903FG_397_18_LINK_E
 334578 CH22_1893FG_406_1_LINK_EM_A
 304621 AA464716
 334616 CH22_1923FG_411_15_LINK_E
 304541 AA462651
 335064 CH22_3440FG_683_3_LINK_DJ
 304735 AA576463
 334981 CH22_2208FG_452_8_LINK_EM_A
 334989 CH22_2216FG_452_13_LINK_E
 305911 AA565686
 334900 CH22_2217FG_452_14_LINK_E
 334902 CH22_2219FG_452_16_LINK_E
 334905 CH22_2222FG_452_20_LINK_E
 334906 CH22_2223FG_452_21_LINK_E
 334961 CH22_2227FG_455_20_LINK_E
 327821 c_5_hs
 330415 19440_1
 D33777 NM_014765 AA339018 DE004425 AL119670 AA323656 DE296006 AL118931 DE266556 AA374227 DE271472 DE296326 AW553557
 AW553529 V14048 AW080433 AA324811 AA150746 AW949991 DE000360 AA362575 DE392178 AA430816 AA348536 AA369534 AW915371
 AA317386 DE072912 DE072917 AA323687 W08796 AA322171 W16951 AA035916 AA330827 AW553515 AA372892 W25430 H07457 AA42389
 AA159592 AA364115 H42160 AA081704 AA775719 A105130 N75556 AW068117 AA964901 AA221199 AA161457 AW511204 AA191639
 N54003 AI337715 AA159219 AA088783 AA548717 AW239470 AW652116 AW156218 D51086 A1887027 AA729243 AI923221 AI357913
 AI375759 AA987267 AA173669 AW500216 AA191460 AA632394 134787 AA627048 C75299 N63172 AW126534 N33415 AJ236459 DE328344
 AW416717 AI363947 H42899 N24773 AA621221 AA917806 AA10855 AA418716 AW95499 AI325276 AI039047 AW553402 AA435500

WO 02/098358

PCT/US02/17594

5	330606	4584_1	A271939 AF978736 AA612803 AW115691 A1183452 AA843085 C65884 C75127 AW044580 T33756 AW15833349 AA028203 AE877439 A2398253 AA010649 AW168981 A1372578 A1003940 A3111909 A3213396 W81554 A1582863 A1566169 AA010546 AA748396 A002365 A074528 AA826701 W65070 A1570312 AA525206 A002069 AA52384 AA895393 A0653378 AA910381 AA967271 AW654327 AW653393 T33040 H02310 A3131354 T11602 A2180310 AW683343 T11569 AA966343 A1719598 A4277283 AA185220 A0800396 A961593 AA01744 A446498 A003516 A353516 A152782 Z88 AA8159 A016130 AW612532 AC064162 A081734 AW693661 AW093559 A384414 AA044953 AA941006 A001735 AA018658 AW92544 T19170
			A130740 A1315123 AW016480 T27986 M61906 A047197 D58003 T21330 AA318686 AA231849 AA075994 AA091104 F05655 W62655 A05461 AA439093 T78213 AA340626 T81988 R14467 AA348986 AA324917 N67834 AA0359582 A00369619 AA0369619 T86645 T79490 A1937019 T81220 R57144 R80283 AA872249 AA330777 AW698484 AA344468 AW0591414 AA22599 H02694 A192744 A446498 T22285 A0175918 R05150 AW080304 A004563 A889740 AA1198022 T29156 T29156 AA0111738 AA0111738 AA017842 A017842 A0173174 T7904 AA661396 AW172868 AW027237 A491392 H141227 A114696 AA044007 A056428 R40036 A1023867 H06371 T279545 R43691 A025160 H05622 H56529 H56628 A1530016 T2645861 A0138559 AA453526 N69643 A04855 AW56092 T15783 H43128 N68131 A132599 H81121 F09171 R44060 H22253 F01172 A0255113 A8344473 H46343 AW070067 A132481 A1937166 AA713487 A423162 AA810839 H45272 AA655114 AW190730 Z44767 F15177 F11518 A035303 H19191 A057810 A058044 AA039163 AW652305 AW530519 A0462905 W51164 T214625 Z11962 R20806 B616740 A019188 AA540628 NM_02038 U22670 U22970 U67364 U09016 Z43999 R11903 R35836 A0002816 AW953298 AW499839 AA499842 B612696 R52743 R12215 AW652701 H02044 W66382 W67694 W09192 AA042691 AV051788 N45261 AV051785 AA370875 B601705 A003610 AA055132 B6018502 B5074256 AV0138381 AA716565 AV051700 AW52528 H48591 A219383 AA808365 AA070049 AW105744 A827700 AA533631 A863453 H11624 A475525 A197929 AW56992 A3531918 A420739 A1564349 AA023166 AA1532369 AA567832 R26259 AA564441 A1330776 R43646 AV0512718 N30919 A054296 N6831 A3173374 H050441 A1687203 N71007 A1274126 A470999 A821324 T33590 A1224462 AA468105 AA907448 AA424516 AA669297 B6148456 R44736 T11890 AA563897 Z3967 H88959 A1368248 F02527 R39697 T36875 AW591246 AA410284 H02820 A4772510 A14042079 B53224 AA0591235 F0227 H06661 A016573 A089149 T30572 H64366 A055535 Z43095 R19394 H16445 H12134 DE24291 AW567794 AW567793 A089242 A0616325 AV051476 AV051476 A0561336 T771796 R742167 R53241 AW1066530 A043982 A265801 AA745252 AA075008 A887214 H80516 AW180337 A1338215 AA469994 A0040616 R82738 N3819 A043637 F05306 A0001546 A868509 A066202 A040140 A0119308 R92384 H86095 H06084 F060624 A002267 H67483 A0935945 AA029860 R63256 AV053877 W44070 AA745749 H61720 A0737094 NM_315228 AA040482 A770690 A001155 A5212554 A219381 A0259953 A219062 A770690 A041229 AA343578 DE543192 A333397 H12165 F11219 R06274 H72204 AW974068 A1819333 AA33635 A060390 A024736 A055046 A24427 A23604 AW022096 R40205 AA56464 F0882 A121140 AA069239 H02546 H72102 T47953 AA472693 A032143 NM_006479 AF008299 A2221623 D244649 A4311615 AA307025 A0960332 A0358100 AA369154 AA629985 AW977244 AA064107 AA047181 AA03059 R77075 AW09294 A002324 A1178 AA190203 A0957423 AA058449 A4311615 A219381 A0259953 A219062 A770690 A041229 AA343578 DE543192 A030399 A068416 A027250 A0611954 A060861 A0185182 A02167 B604763 B688801 A008264 A0600301 AA577538 A0025747 AW52517 B604613 A232231 AW85410 A105520 R76083 AA250728 A053914 A1332395 A0656937 N19605 AW19726 A0278952 A825139 A167770 A151140 B6245117 A030210 A0660707 H09005 A058064 A070363 AA233432 R77725 H40588 A029240 AA048653 A469145 A1853333 A053374 T16956 T16967 DE2239 AW953905 AA651785 A0027526 A022110 AA361304 N661169 A068997 R6807 AA291713 R54971 A7749146 AW96070 AA738719 A0440105 H1205 A021661 NM_1001221 A0259445 H11252 A0045697 D25926 A291817 R6806 AA291783 R14053 A0414879 A0440105 A0440105 H1205 B679354 A192445 A013962 A1744012 A076135 AA047681 A0326222 AA023022 A162785 A1936059 A065171 AW002044 A216555 A13539125 A063506 A0270910 A786930 AW008353 A0552911 AW591147 A0552911 A0552911 A0552911 A0552911 A0552911 AA011558 A052457 A055459 DE21025 A004358 AW151304 A021466 N65178 AA119794 AA024219 AW146507 D05074 A059253 A067957 AA017060 A024167 A1956040 AA170640 AW151704 AA015730 A0054643 A0054637 T02889702 B008888 B003090 A030732 AW03988 A0215297 B651748 AW17355 AA044224 AA351664 AA773328 AW1512704 AA206334 A1307367 A1306293 AA048119 A2118974 AA115431 AW16999 A042009 AW28002 AA043140 AA311781 A0252365 A03171 A027867 R11381 AW02352 A086106 AW467416 AA493914 AA483019 AA443081 A0400751 AA558288 AW070397 AW572838 A053439 A1268564 A0781354 A097254 A171019 DE22191 A015828 AA744724 A0227815 A1131769 AA031641 AA837286 A4737401 A755195 AW08075 AW873024 A587164 AA744556 AA88910 A577276 A032077 AA02955 A002396 AW675991 AA83101 A14A25705 AW139028 AA081819 AA112247 H03109 AA190669 R27719 R77038 R23789 H45171 N43588 R26033 T94741 A111026 AF063500 W35141 AA23629 H1516 AW043845 A053508 A0439683 A0439683 AA112062 AA075968 A0017667 A00514 A007667 A00514 A007667 A00514 A007667 A00514 A007667 A00514 AF102546 AA072738 NM_004392 A1005670 AW079067 A003695 AW579053 AA067265 AW604900 AA090203 A089509 A001001 T11719 R11545 A4219450 AW072022 AW592446 AA064022 A3175131 AA677921 A0012524 A055308 B645771 A122006 D05070 A219357 A011306 R15271 A0211306 A0211306 AW06177 A060062 A06177 A060062 A06177 A060062 A06177 A060062 A06177 A060062 A06177 A060062 A047738 AA115431 AW16999 A042009 AW28002 AA043140 AA311781 A0252365 A03171 A027867 R11381 AW02352 A086106 R44962 A095555 A060041 A0878955 AA479353 A445159 A424124 A086574 A086774 T32446 T16534 AA028117 D63033 AW069291 A071383 A0471359 A003800 A0075978 AA116808 A0075967 A00514 A007667 A00514 A007667 A00514 A007667 A00514 A007667 A00514 A035708 A0439683 A0439683 AA112062 AA075968 A0017667 A00514 A007667 A00514 A007667 A00514 A007667 A00514 A007667 A00514 AF102546 AA072738 NM_004392 A1005670 AW079067 A003695 AW579053 AA067265 AW604900 AA090203 A089509 A001001 T11719 R11545 A4219450 AW072022 AW592446 AA064022 A3175131 AA677921 A0012524 A055308 B645771 A122006 D05070 A219357 A011306 R15271 A0211306 A0211306 AW06177 A060062 A06177 A060062 A06177 A060062 A06177 A060062 A06177 A060062 A06177 A060062 A047738 AA115431 AW16999 A042009 AW28002 AA043140 AA311781 A0252365 A03171 A027867 R11381 AW02352 A086106 R44962 A095555 A060041 A0878955 AA479353 A445159 A424124 A086574 A086774 T32446 T16534 AA028117 D63033 AW069291 A071383 A0471359 A003800 A0075978 AA116808 A0075967 A00514 A007667 A00514 A007667 A00514 A007667 A00514 A007667 A00514 A035708 A0439683 A0439683 AA112062 AA075968 A0017667 A00514 A007667 A00514 A007667 A00514 A007667 A00514 A007667 A00514 AF102546 AA072738 NM_004392 A1005670 AW079067 A003695 AW579053 AA067265 AW604900 AA090203 A089509 A001001 T11719 R11545 A4219450 AW072022 AW592446 AA064022 A3175131 AA677921 A0012524 A055308 B645771 A122006 D05070 A219357 A011306 R15271 A0211306 A0211306 AW06177 A060062 A06177 A060062 A06177 A060062 A06177 A060062 A06177 A060062 A06177 A060062 A047738 AA115431 AW16999 A042009 AW28002 AA043140 AA311781 A0252365 A03171 A027867 R11381 AW02352 A086106 R44962 A095555 A060041 A0878955 AA479353 A445159 A424124 A086574 A086774 T32446 T16534 AA028117 D63033 AW069291 A071383 A0471359 A003800 A0075978 AA116808 A0075967 A00514 A007667 A00514 A007667 A00514 A007667 A00514 A007667 A00514 A035708 A0439683 A0439683 AA112062 AA075968 A0017667 A00514 A007667 A00514 A007667 A00514 A007667 A00514 A007667 A00514 AF102546 AA072738 NM_004392 A1005670 AW079067 A003695 AW579053 AA067265 AW604900 AA090203 A089509 A001001 T11719 R11545 A4219450 AW072022 AW592446 AA064022 A3175131 AA677921 A0012524 A055308 B645771 A122006 D05070 A219357 A011306 R15271 A0211306 A0211306 AW06177 A060062 A06177 A060062 A06177 A060062 A06177 A060062 A06177 A060062 A06177 A060062 A047738 AA115431 AW16999 A042009 AW28002 AA043140 AA311781 A0252365 A03171 A027867 R11381 AW02352 A086106 R44962 A095555 A060041 A0878955 AA479353 A445159 A424124 A086574 A086774 T32446 T16534 AA028117 D63033 AW069291 A071383 A0471359 A003800 A0075978 AA116808 A0075967 A00514 A007667 A00514 A007667 A00514 A007667 A00514 A007667 A00514 A035708 A0439683 A0439683 AA112062 AA075968 A0017667 A00514 A007667 A00514 A007667 A00514 A007667 A00514 A007667 A00514 AF102546 AA072738 NM_004392 A1005670 AW079067 A003695 AW579053 AA067265 AW604900 AA090203 A089509 A001001 T11719 R11545 A4219450 AW072022 AW592446 AA064022 A3175131 AA677921 A0012524 A055308 B645771 A122006 D05070 A219357 A011306 R15271 A0211306 A0211306 AW06177 A060062 A06177 A060062 A06177 A060062 A06177 A060062 A06177 A060062 A06177 A060062 A047738 AA115431 AW16999 A042009 AW28002 AA043140 AA311781 A0252365 A03171 A027867 R11381 AW02352 A086106 R44962 A095555 A060041 A0878955 AA479353 A445159 A424124 A086574 A086774 T32446 T16534 AA028117 D63033 AW069291 A071383 A0471359 A003800 A0075978 AA116808 A0075967 A00514 A007667 A00514 A007667 A00514 A007667 A00514 A007667 A00514 A035708 A0439683 A0439683 AA112062 AA075968 A0017667 A00514 A007667 A00514 A007667 A00514 A007667 A00514 A007667 A00514 AF102546 AA072738 NM_004392 A1005670 AW079067 A003695 AW579053 AA067265 AW604900 AA090203 A089509 A001001 T11719 R11545 A4219450 AW072022 AW592446 AA064022 A3175131 AA677921 A0012524 A055308 B645771 A122006 D05070 A219357 A011306 R15271 A0211306 A0211306 AW06177 A060062 A06177 A060062 A06177 A060062 A06177 A060062 A06177 A060062 A06177 A060062 A047738 AA115431 AW16999 A042009 AW28002 AA043140 AA311781 A0252365 A03171 A027867 R11381 AW02352 A086106 R44962 A095555 A060041 A0878955 AA479353 A445159 A424124 A086574 A086774 T32446 T16534 AA028117 D63033 AW069291 A071383 A0471359 A003800 A0075978 AA116808 A0075967 A00514 A007667 A00514 A007667 A00514 A007667 A00514 A007667 A00514 A035708 A0439683 A0439683 AA112062 AA075968 A0017667 A00514 A007667 A00514 A007667 A00514 A007667 A00514 A007667 A00514 AF102546 AA072738 NM_004392 A1005670 AW079067 A003695 AW579053 AA067265 AW604900 AA090203 A089509 A001001 T11719 R11545 A4219450 AW072022 AW592446 AA064022 A3175131 AA677921 A0012524 A055308 B645771 A122006 D05070 A219357 A011306 R15271 A0211306 A0211306 AW06177 A060062 A06177 A060062 A06177 A060062 A06177 A060062 A06177 A060062 A06177 A060062 A047738 AA115431 AW16999 A042009 AW28002 AA043140 AA311781 A0252365 A03171 A027867 R11381 AW02352 A086106 R44962 A095555 A060041 A0878955 AA479353 A445159 A424124 A086574 A086774 T32446 T16534 AA028117 D63033 AW069291 A071383 A0471359 A003800 A0075978 AA116808 A0075967 A00514 A007667 A00514 A007667 A00514 A007667 A00514 A007667 A00514 A035708 A0439683 A0439683 AA112062 AA075968 A0017667 A00514 A007667 A00514 A007667 A00514 A007667 A00514 A007667 A00514 AF102546 AA072738 NM_004392 A1005670 AW079067 A003695 AW579053 AA067265 AW604900 AA090203 A089509 A001001 T11719 R11545 A4219450 AW072022 AW592446 AA064022 A3175131 AA677921 A0012524 A055308 B645771 A122006 D05070 A219357 A011306 R15271 A0211306 A0211306 AW06177 A060062 A06177 A060062 A06177 A060062 A06177 A060062 A06177 A060062 A06177 A060062 A047738 AA115431 AW16999 A042009 AW28002 AA043140 AA311781 A0252365 A03171 A027867 R11381 AW02352 A086106 R44962 A095555 A060041 A0878955 AA479353 A445159 A424124 A086574 A086774 T32446 T16534 AA028117 D63033 AW069291 A071383 A0471359 A003800 A0075978 AA116808 A0075967 A00514 A007667 A00514 A007667 A00514 A007667 A00514 A007667 A00514 A035708 A0439683 A0439683 AA112062 AA075968 A0017667 A00514 A007667 A00514 A007667 A00514 A007667 A00514 A007667 A00514 AF102546 AA072738 NM_004392 A1005670 AW079067 A003695 AW579053 AA067265 AW604900 AA090203 A089509 A001001 T11719 R11545 A4219450 AW072022 AW592446 AA064022 A3175131 AA677921 A0012524 A055308 B645771 A122006 D05070 A219357 A011306 R15271 A0211306 A0211306 AW06177 A060062 A06177 A060062 A06177 A060062 A06177 A060062 A06177 A060062 A06177 A060062 A047738 AA115431 AW16999 A042009 AW28002 AA043140 AA311781 A0252365 A03171 A027867 R11381 AW02352 A086106 R44962 A095555 A060041 A0878955 AA479353 A445159 A424124 A086574 A086774 T32446 T16534 AA028117 D63033 AW069291 A071383 A0471359 A003800 A0075978 AA116808 A0075967 A00514 A007667 A00514 A007667 A00514 A007667 A00514 A007667 A00514 A035708 A0439683 A0439683 AA112062 AA075968 A0017667 A00514 A007667 A00514 A007667 A00514 A007667 A00514 A007667 A00514 AF102546 AA072738 NM_004392 A1005670 AW079067 A003695 AW579053 AA067265 AW604900 AA090203 A089509 A001001 T11719 R11545 A4219450 AW072022 AW592446 AA064022 A3175131 AA677921 A0012524 A055308 B645771 A122006 D05070 A219357 A011306 R15271 A0211306 A0211306 AW06177 A060062 A06177 A060062 A06177 A060062 A06177 A060062 A06177 A060062 A06177 A060062 A047738 AA115431 AW16999 A042009 AW28002 AA043140 AA311781 A0252365 A03171 A027867 R11381 AW02352 A086106 R44962 A095555 A060041 A0878955 AA479353 A445159 A424124 A086574 A086774 T32446 T16534 AA028117 D63033 AW069291 A071383 A0471359 A003800 A0075978 AA116808 A0075967 A00514 A007667 A00514 A007667 A00514 A007667 A00514 A007667 A00514 A035708 A0439683 A0439683 AA112062 AA075968 A0017667 A00514 A007667 A00514 A007667 A00514 A007667 A00514 A007667 A00514 AF102546 AA072738 NM_004392 A1005670 AW079067 A003695 AW579053 AA067265 AW604900 AA090203 A089509 A001001 T11719 R11545 A4219450 AW072022 AW592446 AA064022 A3175131 AA677921 A0012524 A055308 B645771 A122006 D05070 A219357 A011306 R15271 A0211306 A0211306 AW06177 A060062 A06177 A060062 A06177 A060062 A06177 A060062 A06177 A060062 A06177 A060062 A047738 AA115431 AW16999 A042009 AW28002 AA043140 AA311781 A0252365 A03171 A027867 R11381 AW02352 A086106 R44962 A095555 A060041 A0878955 AA479353 A445159 A424124 A086574 A086774 T32446 T16534 AA028117 D63033 AW069291 A071383 A0471359 A003800 A0075978 AA116808 A0075967 A00514 A007667 A00514 A007667 A00514 A007667 A00514 A007667 A00514 A035708 A0439683 A0439683 AA112062 AA075968 A0017667 A00514 A007667 A00514 A007667 A00514 A007667 A00514 A007667 A00514 AF102546 AA072738 NM_004392 A1005670 AW079067 A003695 AW579053 AA067265 AW604900 AA090203 A089509 A001001 T11719 R1154

PCT/US02/17594

15

WO 02/098358

PCT/US02/17594

5 332577 89088_2
 AW021936 AW118330 AA515368 D56610 AA494092 D56834 T97774 AA473546 R74360 R84834 AA579200 D56616 C03207 D57391 N52416
 D66928 R79208 D56525 AA020879 D46546 A188769 R20750 T03811 F01436 AW627906 D58202 A1933993 F01912 H27552 AA174191
 T16515 AW022126 AA434146 H83387 A1346751 V01512 V01512 AA576407 AW385140 AA937471 BE174681 A1568829 A1274663 R85630
 AL048226 H83388 AW798734
 A1825288 AW248872 H65611 A174806 AW779557 A182254 A1900377 AW151271 A1563574 A1634503 AA777065 A1690131 H13767 A1899658
 H65612 AA045490 N27343 A1573098 AW130956 A1653838 AW069403 AW000790 A1208230 A1273535 AW059294 AA021587 AW734546
 AA050576 AA0465024 AM00222 A1025723 BE046148 A1128668 BE350462 AW303691 A1296977 AA284909 A1640356 AA4770364 A1241794
 AA650048 AW000027 H15377 AW615378 D60021 A1934336 AW118536 A1041281 AA614238 R85810 AW571741 AW516892 AW612232
 A1615189 A1795585 A1352625 Z40516 A1808680 A1468975 A1637919 A1810684 A7071744 A1370410 BE383083 Z44676 BE002481 BE002632
 AA458155 H41196 C00322 C14604 A0021399 A1254872 BE256647 AW045292
 10 332640 4172_1
 BE568452 BE297396 AA440593 AW732490 AW069736 BE548667 AA207229 AF044588 NL 003981 BE268994 AW444578 AA471151
 BE250747 A1732555 AA074582 BE336856 AW008736 A1191159 BE092129 AA310614 A1958677 AA312276 AW750077 AW750046
 AW750032 AW750024 AA188893 AW750054 AW408406 AW750030 BE151875 AA478509 N58721 AA158614 H70079 H75580 BE250401
 AA454516 A4007263 AA526426 AA417152 AA004200 AA567359 AW863181 A102179 A1924143 A1671185 BE006196 AA193630
 A1633736 A1609115 AW65230 BE357023 BE494665 AA463413 BE280968 BE270833 AW229803 A1337375 AA478510 BE011624 A1914763
 A1654726 A1091408 AA827285 AA180108 AW594169 BE116299 BE518040 AL133368 AA632206 A1080126 A1638180 AA725430 A1379107
 A1288872 H14801 A1679151 A1263619 A1559213 A1679722 W93249 AA552345 AA47000 A1659343 AA344544 A1038181 AA766364 AA573241
 A1754375 AW043057 BE207865 A1291838 N73985 N73638 AW060661 AA808510 A1698613 A19168044 A19104716 H58508 AA248270
 BE330222 N56013 AA621595 A1467137 D19371 AW102890 A154283 H73330 A4916989 BE273424 BE560302 AW659012 AA313852
 AW750034 BE072537 BE297947 AW732361 AA448336 C029574
 20 332732 5436_1
 AF191019 NM_015516 BE546454 AL110276 R13844 BE313586 BE336912 R18704 R18703 AA405868 T70952 BE336901 T60387 BE149749
 BE271848 BE271902 AA489929 Z45402 T64360 AA305745 AA009451 T95705 H114907 AA259301 C03221 T72431 AW471185 AA336297
 A0269100 A3435072 AW695160 H27581 R48910 H25330 AA335281 AW673283 T79590 AW185447 T64172 A174097 A1342368 A4356102
 AA335799 BE208375 A1144834 AA686181 A1895314 A778613 T70302 R42877 A1884558 AA469798 A1310929 AA029735 H25381 AW512425
 R48081 H27507 H20105 H44671 A1631362 AA558470 AW014412 AA562069 AA405801 A1558943 AW193657 H14514 AA497425 R42078
 A24578 T61896 A1559202 A1074139 A1871313 A1041484 AA437138 A1613032 A147891 A1457945 AW191727 A1074399 A1578636 A1598048
 AA972877 M65390 R36989 R71936 A1867482 T40081 Z41115 AA772775 T41013 A1656691 T40396 A1828822 N93464 AA665524 AA088651

WO 02/098358

PCT/US02/17594

TABLE 1C

Key: Unique number corresponding to an Ees probe set

Ref: Sequence source. The 7 digit numbers in this column are Genbank Identifier (GI) numbers. "Dunham, I. et al." refers to the publication entitled "The DNA sequence of human chromosome 22." Dunham, I. et al. (1999) *Nature* 402:489-495.

Strand: Indicates DNA strand from which exons were predicted.

Nt_position: Indicates nucleotide positions of predicted exons.

Key	Ref	Strand	Nt_position
332792	Dunham, I. et al.	Plus	73381-73768
333135	Dunham, I. et al.	Plus	3367208-3367369
333137	Dunham, I. et al.	Plus	3367345-3367726
333138	Dunham, I. et al.	Plus	3369205-3369323
333139	Dunham, I. et al.	Plus	3369495-3369571
333516	Dunham, I. et al.	Plus	5570204-5570390
333517	Dunham, I. et al.	Plus	5570729-5570925
333795	Dunham, I. et al.	Plus	7807698-7807795
333796	Dunham, I. et al.	Plus	7808253-7808319
333808	Dunham, I. et al.	Plus	7809600-7809775
333809	Dunham, I. et al.	Plus	7809600-7809775
333845	Dunham, I. et al.	Plus	8065552-8065945
333849	Dunham, I. et al.	Plus	8018323-8018472
334101	Dunham, I. et al.	Plus	9973413-9973550
334616	Dunham, I. et al.	Plus	15176123-15176470
334891	Dunham, I. et al.	Plus	19290778-19295944
334899	Dunham, I. et al.	Plus	19315168-19315311
334900	Dunham, I. et al.	Plus	19315678-19315743
334902	Dunham, I. et al.	Plus	19317093-19317195
334905	Dunham, I. et al.	Plus	19322553-19322680
334905	Dunham, I. et al.	Plus	19323453-19323590
335044	Dunham, I. et al.	Plus	20842088-20842682
335149	Dunham, I. et al.	Plus	21497441-21497587
335809	Dunham, I. et al.	Plus	25310772-25310909
335810	Dunham, I. et al.	Plus	25314767-25314849
335824	Dunham, I. et al.	Plus	25376860-25376942
336054	Dunham, I. et al.	Plus	29161685-29161927
336721	Dunham, I. et al.	Plus	3371522-3371586
337182	Dunham, I. et al.	Plus	23934089-23934982
337674	Dunham, I. et al.	Plus	332516-3332697
337675	Dunham, I. et al.	Plus	3335368-3335505
337755	Dunham, I. et al.	Plus	3971764-3971900
338038	Dunham, I. et al.	Plus	8138219-8138392
338316	Dunham, I. et al.	Plus	17089711-17089868
333124	Dunham, I. et al.	Minus	33119017-3311932
333743	Dunham, I. et al.	Minus	7573216-7573060
334221	Dunham, I. et al.	Minus	12730944-12730387
334222	Dunham, I. et al.	Minus	12732417-12732259
334282	Dunham, I. et al.	Minus	13282593-13283178
334502	Dunham, I. et al.	Minus	14488605-14488626
334578	Dunham, I. et al.	Minus	15004462-15004304
334951	Dunham, I. et al.	Minus	20147708-20147502
335289	Dunham, I. et al.	Minus	22300580-22300705
335290	Dunham, I. et al.	Minus	22300950-22300891
335293	Dunham, I. et al.	Minus	22316408-22316275
335682	Dunham, I. et al.	Minus	25421215-25421093
335753	Dunham, I. et al.	Minus	25761535-25761444
335755	Dunham, I. et al.	Minus	25763800-25763747
335756	Dunham, I. et al.	Minus	25764330-25764251
336662	Dunham, I. et al.	Minus	2158050-2157993
336884	Dunham, I. et al.	Minus	2158050-2157993
337603	Dunham, I. et al.	Minus	1290296-1290194
338561	Dunham, I. et al.	Minus	22311965-22311856
338562	Dunham, I. et al.	Minus	22312594-22312465
339186	Dunham, I. et al.	Minus	32339211-32339067
355889	5867387	Plus	2232529-2232891
330032	6682598	Plus	85171-85237
330033	6682598	Plus	86663-86723
326213	5867224	Minus	60751-60927
326816	6532458	Plus	198354-198436
327110	6117842	Plus	94605-94755
327821	5867965	Plus	313060-313123
328164	5868068	Minus	27080-27225
328640	6004473	Plus	424829-424959
329355	5868538	Minus	107687-107765

Table 2A lists about 1165 genes selected to have an interesting expression pattern during androgen withdrawal of prostate cancer tissue. These genes were selected by analysis of variance, such that the P value is less than 0.01, the 90th percentile exhibits a minimum of 100 average intensity across all samples, and a comparison of any group means shows a minimum 3 fold change. The interesting expression patterns can be broadly defined into the following categories:

1. Genes that are expressed early in the time course of androgen withdrawal, then drop off in expression, and then express again with emergence of androgen-independence (hi-to-lo pattern in table 2A).
2. Genes that are expressed early in the time course, then drop off in expression immediately after androgen-withdrawal, and do not express again with emergence of androgen-independence (hi-to-lo pattern in table 2A).
3. Genes that are expressed early in the time course, then drop off in expression after several days of androgen withdrawal, and do not express again with emergence of androgen-independence (hi-to-lo pattern in table 2A).
4. Genes that are not expressed early in the time course, but express only with emergence of androgen-independence (lo-to-hi pattern in table 2A).
5. Genes that are not expressed early in the time course, but then express as androgen is withdrawn and continue to express with emergence of androgen-independence (lo-to-hi pattern in table 2A).
6. Genes that are not expressed early in the time course, but then express as androgen is withdrawn and drop off again with emergence of androgen-independence (lo-to-hi pattern in table 2A).

Table 2B lists accession numbers for primers lacking a unigenelD in table 2A. For each probe/est is listed a gene cluster number from which oligonucleotides were designed. Gene clusters were compiled using sequences derived from Genbank ESTs and mRNAs. These sequences were clustered based on sequence similarity using Clustering and Alignment Tools (Doolittle et al., Oakland California). Genbank accession numbers for sequences comprising each cluster are listed in the "Accession" column.

Table 2C lists genomic positioning for primers lacking unigenelD and accession numbers in table 2A. For each predicted exon is listed genomic sequence source used for prediction. Nucleotide locations of each predicted exon are also listed.

TABLE 2A: ABOUT 1165 GENES SELECTED TO HAVE AN INTERESTING EXPRESSION PATTERN DURING ANDROGEN WITHDRAWAL OF PROSTATE CANCER TISSUE

Key: Unique Eas probe/est identifier number

ExAcce: Exon/est Accession number, Genbank accession number

UnigenelD: UnigenelD number

Unigene Title: Unigene gene title

Pattern: Broadly defined expression patterns during androgen withdrawal

Key	ExAcce	UnigenelD	Unigene Title	Pattern
433412	AV653729	Hs.18185	CGI-44 protein/sulfide dehydrogenase II	lo-to-hi-to
429097	AQ001270	Hs.195086	hypothetical protein FLJ10408	lo-to-hi-to
442731	A086167	Hs.131044	ESTs	lo-to-hi-to
429820	W25295	Hs.335635	Homo sapiens, clone IMAGE4173482, mRNA	lo-to-hi-to
422267	AB033044	Hs.114012	KIAA1216 protein	lo-to-hi-to
416953	N81537	Hs.263046	ESTs	lo-to-hi-to
413277	H24177	Hs.75262	calhespin O	lo-to-hi-to
417220	AS05661	Hs.60548	hypothetical protein PR01635	lo-to-hi-to
426623	AW974640	Hs.98029	ESTs	lo-to-hi-to
435847	W63621	Hs.39780	CD4017 protein	lo-to-hi-to
443367	AW294013	Hs.200942	ESTs	lo-to-hi-to
443636	AA970705	Hs.131307	ESTs	lo-to-hi-to
404054			Target Exon	lo-to-hi-to
431697	H65740	Hs.38540	ESTs, Weakly similar to ALUA_HUMAN ALU S	lo-to-hi-to
432114	AL035021	Hs.6934	ESTs	lo-to-hi-to
445397	AW275603	Hs.230712	ESTs	lo-to-hi-to
414294	H15266	Hs.31433	ESTs	lo-to-hi-to
424005	AB033041	Hs.137507	veng (van gogh, Drosophila)-like 2	lo-to-hi-to
424401	H67220	Hs.169581	death effector domain-containing	lo-to-hi-to
448749	AB668111	Hs.407590	ESTs	lo-to-hi-to
445356	BS24731	Hs.138627	ESTs	lo-to-hi-to
427221	115449	Hs.174007	von Hippel-Lindau syndrome	lo-to-hi-to
432715	AA247152	Hs.200483	ESTs, Weakly similar to KIAA1074 protein	lo-to-hi-to
425980	AA359551		gibEST177953 Pancreas tumor III Homo sapi	lo-to-hi-to
412492	AW962804		gibEST1374677 MAGE mesenchymal, MAGS Homo	lo-to-hi-to
436882	AA027695		gibEST5602511 NC, CMAP, GCB1 Homo sapiens	lo-to-hi-to
422473	U94780	Hs.117242	meningiomas expressed antigen 8 (colleco-	lo-to-hi-to
404211			NM_005936 Homo sapiens myeloid/lymphoid	lo-to-hi-to
423019	AB40185	Hs.263626	ESTs	lo-to-hi-to
443559	A075785	Hs.263689	ESTs, Moderately similar to ALUB_HUMAN A	lo-to-hi-to
444291	AS060222	Hs.153689	TAF DNA binding protein	lo-to-hi-to
428065	AB34046	Hs.157313	ESTs	lo-to-hi-to
442566	R37337	Hs.12111	ESTs	lo-to-hi-to
442202	BE272862	Hs.106334	hypothetical protein FLJ22625	lo-to-hi-to
430456	A752419	Hs.103914	hypothetical protein FLJ20980	lo-to-hi-to
423476	AL035633		Human DNA sequence from clone RP5-1046G1	lo-to-hi-to
437952	D63209	Hs.5944	solute carrier family 11 (proton-coupled	lo-to-hi-to
451367	AA815092	Hs.77554	Homo sapiens cDNA FLJ14967 fs, clone TH	lo-to-hi-to
454046	AB04732	Hs.259593	ESTs	lo-to-hi-to
444004	N39842	Hs.301444	KIAA1673	lo-to-hi-to
452691	AA164842	Hs.192519	KIAA1600 protein	lo-to-hi-to
434865	AW060449	Hs.116507	ESTs	lo-to-hi-to
440819	AB09444	Hs.202108	ESTs	lo-to-hi-to
413526	AB21695	Hs.135481	ESTs	lo-to-hi-to
422072	AB018255	Hs.111138	KIAA0712 gene product	lo-to-hi-to
453459	BE047032	Hs.257789	ESTs	lo-to-hi-to
419038	AW134924	Hs.190325	ESTs	lo-to-hi-to
413243	AB199286	Hs.193657	gibEST384840 MAGE mesenchymal, MAGL Homo	lo-to-hi-to
432079	AW972748			lo-to-hi-to

WO 02/098358

PCT/US02/17594

	441326	A952794	Hs.159473	ESTs	to-to-hi-to
	441608	R35765	Hs.208132	ESTs, Moderately similar to ALU _U -HUMAN A	to-to-hi-to
	451066	A756660	Hs.208132	ESTs	to-to-hi-to
5	446017	N96238	Hs.55185	ESTs	to-to-hi-to
	447104	R15365	Hs.210706	Homo sapiens cDNA FLJ13162 fls, clone NT	to-to-hi-to
	447211	A.161861	Hs.17787	KIAA1554 protein	to-to-hi-to
	447765	AW014112	Hs.161390	ESTs	to-to-hi-to
	428540	M55776	Hs.161390	glc:EST02297 Fetal brain, Stralagene (col	to-to-hi-to
10	444314	A1404507	Hs.76422	glc:aw16095a.1 Soares_fetal_liver_spleen_	to-to-hi-to
	414555	N95595	Hs.278611	phospholipase A2, group 1A (pholipase,	to-to-hi-to
	432677	NM_004482	Hs.278611	UDP-N-acetyl-alpha-D-galactoseamineopolyp	to-to-hi-to
	422091	A906339	Hs.97927	ESTs	to-to-hi-to
	423026	H90648	Hs.162952	ghy:66022.r1 Soares fetal liver spleen	to-to-hi-to
	444040	A7204231	Hs.126594	gdnf-47	to-to-hi-to
15	441111	A909667	Hs.126594	ESTs	to-to-hi-to
	416836	AW365224	Hs.36198	ectonucleotide pyrophosphatase/phosphodi	to-to-hi-to
	415599	AA172179	Hs.254029	ESTs	to-to-hi-to
	429615	A7265627	Hs.211562	ATP-binding cassette, sub-family A (ABC1	to-to-hi-to
20	427774	A4276563	Hs.160737	Homo sapiens clone Z3954 and Z3955 mRNA	to-to-hi-to
	435655	AA611371	Hs.123362	ESTs	to-to-hi-to
	424776	A1667931	Hs.164595	ESTs	to-to-hi-to
	413766	AW613760	Hs.13800	ESTs	to-to-hi-to
	421077	AQ000261	Hs.101550	hypothetical protein	to-to-hi-to
25	446837	A261700	Hs.145844	ESTs	to-to-hi-to
	449262	AL048096	Hs.23437	Homo sapiens cDNA FLJ13555 fls, clone PL	to-to-hi-to
	414065	AW515373	Hs.271249	Homo sapiens cDNA FLJ13580 fls, clone PL	to-to-hi-to
	432627	AW575028	Hs.102754	ESTs	to-to-hi-to
	412052	BE242651	Hs.14547	ESTs	to-to-hi-to
30	457121	A7433770	Hs.180513	ESTs, Weakly similar to KIAA0822 protein	to-to-hi-to
	417260	AW173116	Hs.250108	ESTs	to-to-hi-to
	452445	A3002436	Hs.25598	Homo sapiens mRNA from chromosome Sq21-2	to-to-hi-to
	438624	AA589055	Hs.123486	ESTs	to-to-hi-to
	442943	AA352480	Hs.125674	ESTs	to-to-hi-to
35	401416			C14000338.gi1456502.p1rj574665 outer	to-to-hi-to
	437176	AW178909	Hs.42346	calcineurin-binding protein calcasarin-1	to-to-hi-to
	461863	A1872360	Hs.205253	ESTs	to-to-hi-to
	442955	AW137266	Hs.270564	ESTs	to-to-hi-to
	426948	I72531	Hs.36190	ESTs	to-to-hi-to
40	445467	A1239632	Hs.15617	ESTs, Weakly similar to ALU _U -HUMAN ALU S	to-to-hi-to
	416962	AB01098	Hs.151500	ESTs	to-to-hi-to
	416239	AL050450	Hs.48949	ESTs	to-to-hi-to
	429524	AA589698	Hs.20919	ESTs	to-to-hi-to
	435264	AA675470	Hs.96649	Homo sapiens cDNA FLJ11492 fls, clone HE	to-to-hi-to
45	424332	AA338919	Hs.101615	ESTs	to-to-hi-to
	442369	A956071	Hs.125563	ESTs	to-to-hi-to
	420717	A4264447	Hs.271837	ESTs	to-to-hi-to
	439584	AA839114	Hs.221612	ESTs	to-to-hi-to
	440260	A972667	Hs.7130	copine IV	to-to-hi-to
50	426269	H15302	Hs.165520	Homo sapiens mRNA; cDNA DKFZp666A1046 (I	to-to-hi-to
	425399	A424366	Hs.96358	ESTs	to-to-hi-to
	407276	AB511116	Hs.329736	Homo sapiens breast cancer antigen NY-BR	to-to-hi-to
	409339	AB020686	Hs.54037	ectonucleotide pyrophosphatase/phosphodi	to-to-hi-to
	442150	A568158	Hs.70983	PTPL1-associated RhoGAP 1	to-to-hi-to
55	415767	H01463	Hs.53534	ESTs	to-to-hi-to
	432665	A892234	Hs.191666	ESTs, Weakly similar to GNMSLL retrovira	to-to-hi-to
	443764	IN54104	Hs.25260	ESTs	to-to-hi-to
	446215	AW621329	Hs.14366	SH3 domain binding glutamic acid-rich pr	to-to-hi-to
	441265	NM_002374	Hs.167	microtubule-associated protein 2	to-to-hi-to
60	444734	BE614061		gh:01503815F1 NH1_MSC_71 Homo sapiens c	to-to-hi-to
	403746			ENSP00000228612-KIAA1404 protein (Fragm	to-to-hi-to
	434022	R16374	Hs.117966	ESTs	to-to-hi-to
	436714	AA699325	Hs.256660	ESTs	to-to-hi-to
	435646	AW579249		gh:EST391359 MAGC, nonreducing, MAGP Homo	to-to-hi-to
65	421574	A4302170	Hs.17602	gh:EST114192 Testis tumor Homo sapiens c	to-to-hi-to
	433332	A367347	Hs.44696	Homo sapiens clone TCCTCA00151 mRNA seque	to-to-hi-to
	449919	A674665	Hs.200141	ESTs	to-to-hi-to
	407192	AA602200		gh:af12a02a.1 Soares_testis_NIT1 Homo sap	to-to-hi-to
	435169	AA563311	Hs.17602	Homo sapiens cDNA FLJ12361 fls, clone MA	to-to-hi-to
70	419624	A0734020	Hs.104211	ESTs	to-to-hi-to
	432432	AA541323	Hs.115631	ESTs	to-to-hi-to
	426172	AA371307	Hs.125066	ESTs	to-to-hi-to
	401033			C1200556P.gi3330167.phy:AA86477.1 (A	to-to-hi-to
	429716	NM_006375	Hs.171521	scara domain, immunoglobulin domain (Ig),	to-to-hi-to
75	439569	AW602166	Hs.222359	CEGP1 protein	to-to-hi-to
	451720	AW970565	Hs.250653	ESTs	to-to-hi-to
	425163	AA584766		gh:am20a10.1 Soares_NFL_T_GBC_S1 Homo s	to-to-hi-to
	433435	BE171866	Hs.262070	ESTs	to-to-hi-to
	406170	AW004516	Hs.31635	ESTs	to-to-hi-to
80	433530	BE349534	Hs.261769	ESTs	to-to-hi-to
	425776	U25126	Hs.159499	parathyroid hormone receptor: 2	to-to-hi-to
	403068	AA464864		gh:ex0101.1 Soares ovary tumor NBH0T1 H	to-to-hi-to
	427225	A4315703	Hs.155553	ESTs, Weakly similar to ALU _U -HUMAN III	to-to-hi-to

WO 02/098358

PCT/US02/17594

5	432314	AA533447	Ha.312688	ESTs	to-to-hi-to
	434609	R78553		gby66cl1.1 Source placenta Nb2H Homo	to-to-hi-to
	448760	AA313825	Ha.21941	AD036 protein	to-to-hi-to
	417381	AF164142	Ha.28042	solute carrier family 23 (nucleoside tra	to-to-hi-to
10	465334	T60392	Ha.271745	ESTs	to-to-hi-to
	435446	AAT73345	Ha.260441	ESTs	to-to-hi-to
	411928	AA88624	Ha.197289	rab3 GTPase-activating protein, non-cata	to-to-hi-to
	438869	AF075009		gbr1 homo sapiens full length insert cDNA	to-to-hi-to
15	423932	T95633	Ha.188703	ESTs	to-to-hi-to
	422222	A1893072	Ha.155247	hypothetical protein DK5Zp434A171	to-to-hi-to
	434641	AW073202	Ha.334625	Homo sapiens cDNA FLJ14752 fs, clone NT	to-to-hi-to
	415736	AA827082	Ha.291872	ESTs	to-to-hi-to
20	432722	AA830532	Ha.326150	ESTs	to-to-hi-to
	435511	AA863336	Ha.189046	ESTs	to-to-hi-to
	432842	AW022716	Ha.167660	ESTs, Weakly similar to ALU4_HUMAN ALU S	to-to-hi-to
	451141	AW772713	Ha.247186	ESTs	to-to-hi-to
25	450646	AA010200	Ha.178551	ESTs	to-to-hi-to
	413351	BE196815		ESTs	to-to-hi-to
	439334	AF066134	Ha.54309	ESTs	to-to-hi-to
	452685	AA721140	Ha.49590	ESTs, Weakly similar to putative p150 [H	to-to-hi-to
30	415669	NM_005025	Ha.78888	serine (or cysteine) proteinase inhibitor	to-to-hi-to
	450164	A0239523	Ha.63831	ESTs	to-to-hi-to
	417165	R13650	Ha.248773	ESTs	to-to-hi-to
	435645	R36475	Ha.24321	Homo sapiens cDNA FLJ12028 fs, clone HE	to-to-hi-to
35	424878	HE7111	Ha.221132	ESTs	to-to-hi-to
	445616	A075459	Ha.16878	KAA1272 protein	to-to-hi-to
	432672	A860840	Ha.151202	ESTs, Weakly similar to ALU6_HUMAN III	to-to-hi-to
	402953	HS1002	Ha.305480	Homo sapiens mRNA; cDNA DKFZp751E1212 (f	to-to-hi-to
40	431474	AL133590	Ha.150542	CEGP1 protein	to-to-hi-to
	421674	T10707	Ha.286355	hypothetical protein FLJ23138	to-to-hi-to
	438454	AA508678	Ha.310183	ESTs	to-to-hi-to
	425332	AA633306	Ha.127279	ESTs	to-to-hi-to
45	461411	A1077462	Ha.135655	EST	to-to-hi-to
	415972	AL041465	Ha.125992	polg'n-67	to-to-hi-to
	434504	AA645890	Ha.348146	gbns4405.s1 NCL_OGAP_Ak1 Homo sapiens	to-to-hi-to
	424832	AW026680	Ha.253565	ESTs, Moderately similar to PCA255 ferri	to-to-hi-to
50	408660	A452575	Ha.253565	ESTs, Moderately similar to PCA255 ferri	to-to-hi-to
	432674	AA641052	Ha.257339	ESTs, Weakly similar to I38022 (hypotheti	to-to-hi-to
	448150	AW72167		ESTs	to-to-hi-to
	450466	AW75075	Ha.141742	Homo sapiens cDNA FLJ12211 fs, clone MA	to-to-hi-to
55	452674	A0307051	Ha.33526	hypothetical protein FLJ10189	to-to-hi-to
	412086	A859466	Ha.108632	ESTs	to-to-hi-to
	443451	A067404	Ha.56856	ESTs	to-to-hi-to
	435653	AL040600	Ha.168053	ESTs	to-to-hi-to
60	415863	AW552651	Ha.93465	Homo sapiens mRNA; cDNA DKFZp751D151 (H	to-to-hi-to
	427725	AW554697	Ha.250325	ESTs	to-to-hi-to
	440501	AA503666	Ha.150535	ESTs	to-to-hi-to
	407284	AJ355227	Ha.214039	hypothetical protein FLJ23556	to-to-hi-to
65	426279	AA425310	Ha.155766	ESTs, Weakly similar to A47592 B-cell gr	to-to-hi-to
	436602	A0215140		ESTs, Moderately similar to ALU6_HUMAN A	to-to-hi-to
	432340	A434222		gby12162.s1 NCL_OGAP_A41 Homo sapiens	to-to-hi-to
	442048	AA574603		gbop3405.s1 Sources_NFL_T_GBC_S1 Homo s	to-to-hi-to
70	418781	T41160	Ha.8404	ESTs	to-to-hi-to
	450542	R35713	Ha.7130	cephe IV	to-to-hi-to
	451691	A023650	Ha.267777	Homo sapiens, Similar to KGA00643 prot	to-to-hi-to
	435812	AA700439	Ha.188460	ESTs	to-to-hi-to
75	446065	A1455177	Ha.172769	ESTs, Moderately similar to ALU7_HUMAN A	to-to-hi-to
	453438	AL035201	Ha.173554	ubiquinol-cytochrome c reductase core pr	to-to-hi-to
	414512	AA155594	Ha.191080	ESTs	to-to-hi-to
	435840	AW023384		gbr11-HF-BR0p aka 4-12-O-NIL-r1 NLM_MGC_5	to-to-hi-to
80	408001	AA046468	Ha.95296	ESTs	to-to-hi-to
	421476	AW563805	Ha.21887	ESTs	to-to-hi-to
	414426	D60745	Ha.255225	Homo sapiens, clone MGC15553, mRNA, com	to-to-hi-to
	444593	HS1057	Ha.264123	AW042N protein	to-to-hi-to
85	418771	AA807881	Ha.25329	ESTs	to-to-hi-to
	417845	W07361	Ha.22545	Homo sapiens cDNA FLJ12635 fs, clone NT	to-to-hi-to
	415556	AA642445	Ha.48264	ESTs, Weakly similar to AF151800 1 CG-4	to-to-hi-to
	415226	A027237	Ha.282664	ESTs	to-to-hi-to
90	415905	AW046229	Ha.53655	protein disulfide isomerase related prot	to-to-hi-to
	452870	AW602761	Ha.30505	KAA0430 gene product	to-to-hi-to
	440059	AK000566	Ha.58135	hypothetical protein FLJ20569	to-to-hi-to
	411517	NM_003243	Ha.342674	transforming growth factor, beta receptor	to-to-hi-to
95	425306	AW553845	Ha.95056	hypothetical protein FLJ23558	to-to-hi-to
	419235	AAW70411	Ha.288433	neurotrophin	to-to-hi-to
	416640	BE252478	Ha.75404	neuron-specific protein	to-to-hi-to
	434838	AW000718	Ha.81515	Homo sapiens, clone MGC16165, mRNA, com	to-to-hi-to
100	405177	A041733	Ha.438171	ESTs	to-to-hi-to
	438459	TA0300	Ha.35304	Homo sapiens cDNA FLJ13555 fs, clone PL	to-to-hi-to
	418381	AA682355		ESTs	to-to-hi-to
	432161	AK000400	Ha.341181	ESTs, Weakly similar to envelope [LSpap	to-to-hi-to
105	415283	S79695	Ha.83542	cathepsin K (pyridoxalase)	to-to-hi-to
	421443	BE550141	Ha.155145	hypothetical protein FLJ13231	to-to-hi-to

[illegible]

WO 02/098358

PCT/US02/17594

	400111		Fire Control	
	405446	A1015709	Homo sapiens mRNA; cDNA DKFZp6882022 g	
	401563		C13001262g[7304681]ref[NP_038526.1]ca	
5	402786		C1000887g[12732463]ref[QF_011474.1]C	
	425464	AAS37658	KAA1467 protein	
	414343	AL038166	coated vesicle membrane protein	
	421970	AF227156	RNA polymerase I transcription factor RR	
	422592	BE081857	rcd1 (required for cell differentiation,	
10	413431	AW246428	ubiquitin-conjugating enzyme E2N (homolo	
	425746	J30626	uridine monophosphate synthetase (bact	
	402037		NM_001087*Homo sapiens: angio-associated	
	402532		Target Exon	
	402396		Target Exon	
15	458649	AW298364	ESTs	
	401512		NM_014080:Homo sapiens dual oxidase-like	
	448622	AL046508	ESTs, Weakly similar to STK2_HUMAN SERIN	
	400501		ENSP00000251912*GAA1617 protein (Fragm	
	452324	W81406	ESTs	
20	451746	A339552	ESTs	
	430446	AW82432	ESTs	
	401750		NM_012448*Homo sapiens: signal transduce	
	436286	T03960	ESTs, Highly similar to ARX_MOUSE HOMEOD	
	400575	NM_014115	NM_014115*Homo sapiens: PRO0113 protein	
25	417151	AA109529	Homo sapiens cDNA: FLJ221800 fis, clone L	
	410498	AA355749	gb:EST64455 Jankai: T-cells V1.Homo sapie	
	405044		NM_014630*Homo sapiens: KIAA0211 gene pr	
	415169	AW161061	ESTs, Weakly similar to zinc finger prot	
	402101		ENSP0000021722*Lambda alpha-1 chain p	
30	418508	AW850818	gb:U3-CTG226-091189-026-AG3 CTG202*Homo	
	446826	AK000626	hypothetical protein FLJ20619	
	412180	AW859751	gb:CMO-NN0075-130400-332-406 NN0075 Homo	
	407273	AJ132560	gb:Homo sapiens: mRNA for immunoglobulin	
	452656	BE138229	phosphomonomate kinase	
	416117	H19480	ESTs	
35	430834	AT952302	potassium inwardly-rectifying channel, s	
	418309	R84694	cAMP responsive element binding protein	
	444678	T80795	ESTs	
	401966		C17000574.g[8823190]ref[NP_060178.1]hy	
40	444650	AW444882	ESTs	
	403986		Target Exon	
	495435		Target Exon	
	422694	C06003	Hypothetical protein FLJ12847	
	422912	AW405973	ESTs	
45	412748	BE083158	Homo sapiens cDNA: FLJ23313 fis, clone H	
	403704		Target Exon	
	445507	H06894	gb:U11607.1 Soares Infant: brain TMB H	
	405503		C7000609.g[8160212]p[AS3333 myosin I	
	456123	R00602	gb:yo74c04.1 Soares fetal liver spleen	
50	454261	AF216077	Homo sapiens clone HB-2 mRNA sequence	
	458596	BE220675	gb:U10911.1 NCI_CGAP: Lnc24 Homo sapiens	
	418367	AA326036	hypothetical protein DKFZp434L0716	
	444653	A1187530	ESTs	
	406811		NM_024810*Homo sapiens: hypothetical prot	
55	426461	A188216	ESTs, Weakly similar to HSR2_HUMAN DNAJ	
	423378	BE113601	hypothetical protein FLJ22556	
	458516	BE010749	ESTs	
	404039		ENSP00000247650*Hypothetical 177.6 kDa	
	454148	AW732837	nasopharyngeal carcinoma susceptibility	
60	412878	AA116575	ESTs	
	442298	AB11333	ESTs	
	405526		NM_002435*Homo sapiens: mlt5 (E. coli) h	
	424576	BE154142	ESTs	
	451601	R92100	embosional protein 1	
65	422385	AA130177	DKFZp434G0335 protein	
	434333	AA186733	stromal cell protein	
	413509	BE145419	gb:U15-HT0158-291059-009-E01 HT0108 Homo	
	416504	AD86585	ESTs	
	444596	AF285120	CGI-204 protein	
70	401209		C12000619.g[7700045]ref[NP_057014.1]ki	
	423554	M05516	glutamine-fructose-6-phosphate transamin	
	439803	AA001021	thyroid hormone receptor interactor 2	
	424653	AA343728	gb:EST149730 Gall: Interactor 1 Homo sapiens	
	408122	A432362	hypothetical protein -LJ10716	
75	408958	NM_0015123	hyaluronan synthase 1	
	408214	AL120446	hypothetical protein FLJ21343	
	421511	AL041520	gb:DKFZp434G0337_s1_434 (synonym: hies3)	
	407813	AL120247	KAA0872 protein	
	425211	M18667	prostaglandin (prostaglandin C)	
	442772	AW503680	Homo sapiens clone 24416 mRNA sequence	
80	418733	AW362865	Homo sapiens cDNA FLJ114115 fis, clone HE	
	428260	AW230896	ESTs, Weakly similar to S85657 alpha-1C-	
	427683	NM_005363	Sec23 (S. cerevisiae) homolog B	

WO 02/098358

PCT/US02/17594

15853	AA604379	Hs.86211	hypothetical protein	to-to-hi-hi
47355	AA846203	Hs.193874	ESTs, Weakly similar to ALU1_HUMAN ALU S	to-to-hi-hi
454003	AA058544	Hs.116602	Homo sapiens, clone IMAGE:4154008, mRNA,	to-to-hi-hi
423522	U63630	Hs.155637	protein kinase, DNA-activated, catalytic	to-to-hi-hi
42240			Target Exon	to-to-hi-hi
421857	AA481078	Hs.109045	hypothetical protein FLJ10498	to-to-hi-hi
408603	R25283	Hs.325416	Homo sapiens mRNA; cDNA DKFZp564H1516 jf	to-to-hi-hi
437389	AL355587	Hs.271586	hypothetical protein DKFZp72M115	to-to-hi-hi
457149	AF051035	Hs.184627	KIAA0118 protein	to-to-hi-hi
400277			Est Contig	to-to-hi-hi
400955			C11002595.g[12737/273]cd[XP_012163.1]	to-to-hi-hi
400818			Target Exon	to-to-hi-hi
402758			C1001895.g[1272263]cd[XP_010672.1]c	to-to-hi-hi
453708			Target Exon	to-to-hi-hi
408610			ENSP000002410595.cDNA	to-to-hi-hi
414242	AA749230	Hs.26433	dolichyl-phosphate (UDP-N-acetylglucosam	to-to-hi-hi
420757	X78592	Hs.59815	androgen receptor (dihydrotestosterone r	to-to-hi-hi
402665			C110021957.g[12757/273]cd[XP_012163.1]	to-to-hi-hi
401192			Target Exon	to-to-hi-hi
404407			Target Exon	to-to-hi-hi
401405			Target Exon	to-to-hi-hi
403065			C20022193.g[1273728]cd[XP_006682.2]k	to-to-hi-hi
404651			C5000339.g[1273728]cd[XP_006682.2]k	to-to-hi-hi
433627	AF078856	Hs.284266	Homo sapiens cDNA: FLJ22955 fs, clone K	to-to-hi-hi
410204	AJ243425	Hs.326035	early growth response 1	to-to-hi-hi
432642	BE257635	Hs.3069	heat shock 70MD protein 5B (morfa1n-2)	to-to-hi-hi
400765			Target Exon	to-to-hi-hi
432660	AA137152	Hs.286049	phosphoserine aminotransferase	to-to-hi-hi
403725			Target Exon	to-to-hi-hi
413587	AA156164	Hs.286241	protein kinase, cAMP-dependent, regulatory	to-to-hi-hi
422614	A090806	Hs.293362	Homo sapiens cDNA FLJ14459 fs, clone HE	to-to-hi-hi
400275			NM_004613?Homo sapiens seryl-tRNA synth	to-to-hi-hi
402610			NM_004613?Homo sapiens capping protein	to-to-hi-hi
452049	BE268289	Hs.27693	pep[di]prolyl isomerase (cyclophilin-1	to-to-hi-hi
445677	H95577	Hs.5838	ras homolog gene family, member E	to-to-hi-hi
428770	AK011667	Hs.193328	hypothetical protein FLJ10805	to-to-hi-hi
422403	AJ293046	Hs.326159	leucine rich repeat (in FLJ) interact	to-to-hi-hi
434647	W074159	Hs.103189	[popo]ysaccharide specific response-68	to-to-hi-hi
402807			ENSP000002352295.EMB	to-to-hi-hi
413592	W62276	Hs.136075	RNA, U2 small nuclear	to-to-hi-hi
407191	AA069751		glna65b07.s1 Small antigen lung carcinoma	to-to-hi-hi
403329			Target Exon	to-to-hi-hi
411984	NM_005419	Hs.72868	signal transducer and activator of trans	to-to-hi-hi
451017	BE391847	Hs.181173	hypothetical protein MGC10771	to-to-hi-hi
404108			C7000511.g[4235142]gb[AAD14470.1] (ACD	to-to-hi-hi
407819	RA2185	Hs.102720	ESTs	to-to-hi-hi
433876	AW612896	Hs.160271	G protein-coupled receptor 46	to-to-hi-hi
436716	AA33540		glna65b05.s1 NCL_GCAP_1Gd11 Homo sapien	to-to-hi-hi
401419			Target Exon	to-to-hi-hi
424363	AW512144	Hs.346947	ESTs, Weakly similar to A48808 carboxyle	to-to-hi-hi
408865	AW252096	Hs.255036	ESTs	to-to-hi-hi
418516	F11411		glna65b05.s1 NCL_GCAP_1Gd11 Homo sapien	to-to-hi-hi
423144	AW651527	Hs.253677	ESTs, Weakly similar to B3022 hypotheti	to-to-hi-hi
426250	BE077064	Hs.59869	ESTs	to-to-hi-hi
430827	AA946536	Hs.187369	ESTs	to-to-hi-hi
418705	AA255592	Hs.347673	ESTs, Weakly similar to alternatively sp	to-to-hi-hi
413672	BE155636		glna65b05.s1 NCL_GCAP_1Gd11 Homo sapien	to-to-hi-hi
425281	AA354572		glna65b05.s1 NCL_GCAP_1Gd11 Homo sapien	to-to-hi-hi
427403	AA402107	Hs.257146	ESTs, Moderately similar to B3022 hypoth	to-to-hi-hi
430911	AW537461	Hs.255377	ESTs	to-to-hi-hi
435293	AA040777	Hs.117170	ESTs	to-to-hi-hi
444959	AJ523857	Hs.271692	ESTs, Weakly similar to B3022 hypotheti	to-to-hi-hi
445639	W00363	Hs.58446	ESTs	to-to-hi-hi
468092	AW578811	Hs.314451	ESTs, Weakly similar to ALU1_HUMAN ALU S	to-to-hi-hi
459407	N92114		glna65b05.s1 NCL_GCAP_1Gd11 Homo sapien	to-to-hi-hi
423321	AA323486	Hs.271273	Homo sapiens cDNA FLJ12335 fs, clone MA	to-to-hi-hi
450628	AW382884	Hs.204715	ESTs	to-to-hi-hi
411650	AA655253	Hs.130075	RNA, U2 small nuclear	to-to-hi-hi
414735	U83967	Hs.77156	spectrin, alpha, non-erythrocytic 1 (alp	to-to-hi-hi
444165	AV648170	Hs.58756	ESTs	to-to-hi-hi
426111	U77413	Hs.100293	O-linked N-acetylglucosamine (GlcNAc) tr	to-to-hi-hi
427155	AB007393	Hs.112082	KIAA0443 gene product	to-to-hi-hi
457204	AA027823	Hs.145424	Homo sapiens PNAS: cDNA, complete cds	to-to-hi-hi
426074	AA495930		Homo sapiens cDNA: FLJ22155 fs, clone H	to-to-hi-hi
426376	NA6752	Hs.302985	ESTs	to-to-hi-hi
447754	AW073310	Hs.163533	Homo sapiens cDNA FLJ14142 fs, clone MA	to-to-hi-hi
414594	AA452513	Hs.71404	ESTs	to-to-hi-hi
449010	U69650	Hs.3826	valch-like protein CSBP1	to-to-hi-hi
430064	AK000091	Hs.231436	hypothetical protein FLJ20094	to-to-hi-hi
412205	N33818	Hs.20274	ESTs, Weakly similar to unnamed protein	to-to-hi-hi
422955	AA240582	Hs.136164	cutaneous T-cell lymphoma-associated tum	to-to-hi-hi
459615	BE063853		glna65b05.s1 NCL_GCAP_1Gd11 Homo sapien	to-to-hi-hi

WO 02/098358

PCT/US02/17594

	408722	AA467860	Hs.298102	ESTs	lo-to-hi-hi
	455710	AD71896	Hs.121892	ESTs	lo-to-hi-hi
	417518	AA309205	Hs.163754	hypothetical protein FLJ26095	lo-to-hi-hi
5	402964			NM_022095? Homo sapiens hypothetical C2H	lo-to-hi-hi
	424387	AT39312	Hs.284163	ANG-ZEN protein	lo-to-hi-hi
	427220	AF098617	Hs.173993	RNA binding motif protein 6	lo-to-hi-hi
	110451	BE056587		gb:RCS-8T0316-270400-015 f10 BT0316 Homo	lo-to-hi-hi
	400713			NM_005165? Homo sapiens nuclear factor 1	lo-to-hi-hi
10	407218	AA095473	Hs.28505	ubiquitin-conjugating enzyme E2H (homolog)	lo-to-hi-hi
	449312	NT1673	Hs.223666	ESTs	lo-to-hi-hi
	411961	AA06267	Hs.110613	KIAA0421 protein	lo-to-hi-hi
	453272	BE148152		gb:RCA-HT0231-041199-012.b04 HT0231 Homo	lo-to-hi-hi
	401839			NM_005177? Homo sapiens AT1 Para, 11-trans	lo-to-hi-hi
	440422	AW452696	Hs.130760	myosin phosphatase, target subunit 2	lo-to-hi-hi
15	436819	AA731746	Hs.120232	ESTs	lo-to-hi-hi
	413844	BE154810	Hs.278793	ESTs, Weakly similar to Z195_HUMAN ZINC	lo-to-hi-hi
	413939	AL047051	Hs.195981	ESTs, Weakly similar to ALU7_HUMAN ALU S	lo-to-hi-hi
	448198	BE622100	Hs.209405	ESTs, Weakly similar to I38600 zhu flag	lo-to-hi-hi
20	450488	AA009999	Hs.59159	ESTs, Moderately similar to HPV16 E1 pro	lo-to-hi-hi
	433527	AI617336	Hs.191791	ESTs	lo-to-hi-hi
	438966	AW745336	Hs.110613	KIAA0421 protein	lo-to-hi-hi
	442789	AW904361	Hs.131191	ESTs, Weakly similar to ALU7_HUMAN ALU S	lo-to-hi-hi
	407251	U67511		transaldolase 1	lo-to-hi-hi
25	409051	AA063912		gb:zm04003.1 Stralagene hNT neuron (937	lo-to-hi-hi
	409123	AA063403		gb:zm04012.1 Stralagene corneal stroma	lo-to-hi-hi
	416225	AA577730	Hs.188684	ESTs, Weakly similar to PC4259 fertilin	lo-to-hi-hi
	433735	AA068955	Hs.109653	ESTs	lo-to-hi-hi
	434404	AW445034	Hs.226578	ESTs	lo-to-hi-hi
	446667	BE151878	Hs.224806	ESTs	lo-to-hi-hi
30	447982	I22963	Hs.127651	ESTs	lo-to-hi-hi
	438980	AA827756	Hs.135049	ESTs, Weakly similar to ALU7_HUMAN ALU S	lo-to-hi-hi
	427882	AA640987	Hs.193767	ESTs	lo-to-hi-hi
	459690	H96882	Hs.42321	ESTs	lo-to-hi-hi
35	416532	W09490	Hs.141304	ESTs	lo-to-hi-hi
	453876	AW021748	Hs.110400	ESTs, Weakly similar to I38022 hypophell	lo-to-hi-hi
	414528	AA148950	Hs.188836	ESTs	lo-to-hi-hi
	419502	AA804409	Hs.118920	ESTs	lo-to-hi-hi
	405542	AA553020	Hs.30663	hypothetical protein FLJ22418	lo-to-hi-hi
40	435480	AG25195	Hs.130951	hypothetical protein MGC4400	lo-to-hi-hi
	447499	AV025280	Hs.147574	prothymosin beta 15	lo-to-hi-hi
	436023	AI892552		gb:wf3812.1 NCL_GCAP_Lu24 Homo sapiens	lo-to-hi-hi
	412158	H29487	Hs.171110	Homo sapiens mRNA; cDNA DKF2p434C2016 (f	lo-to-hi-hi
	414505	R45599	Hs.23358	ESTs, Weakly similar to A49042 lysosomal	lo-to-hi-hi
45	440477			NM_019111? Homo sapiens major histocompa	lo-to-hi-hi
	414662	AL036058	Hs.76807	major histocompatibility complex, class	lo-to-hi-hi
	444430	AI611153	Hs.6093	Homo sapiens cDNA: FLJ22783 fis, clone K	lo-to-hi-hi
	445512	N94128	Hs.12969	hypothetical protein	lo-to-hi-hi
	407139			ENSP000002555? UOP-glucosyltransferase	lo-to-hi-hi
50	403740			NM_001079? Homo sapiens UOP glycosyltr	lo-to-hi-hi
	411084	T18987	Hs.125472	ESTs, Moderately similar to KIAA0877 pro	lo-to-hi-hi
	429143	AA333327	Hs.197335	plasma glutamate carboxypeptidase	lo-to-hi-hi
	413620	CT6874	Hs.8944	procollagen C-endopeptidase enhancer 2	lo-to-hi-hi
	422748	W01078	Hs.278573	C259 antigen p18-20 (antigen identified	lo-to-hi-hi
55	429441	AJ224172	Hs.204096	lipophilin B (steroid-binding family member)	lo-to-hi-hi
	414382	AW380339	Hs.8068	hematopoietic PBX-interacting protein	lo-to-hi-hi
	415160	F13398	Hs.7888	Homo sapiens clone 23736 mRNA sequence	lo-to-hi-hi
	440106	AS377165	Hs.124834	ESTs	lo-to-hi-hi
	452239	AW375378	Hs.170121	protein tyrosine phosphatase, receptor 1	lo-to-hi-hi
60	446874	AW668304	Hs.56156	ESTs	lo-to-hi-hi
	412795	BE241753	Hs.145592	special AT-rich sequence binding protein	lo-to-hi-hi
	430325	AF004562	Hs.239356	synuclein binding protein 1	lo-to-hi-hi
	426392	AW668324	Hs.17384	ESTs	lo-to-hi-hi
	447448	BE244285		F-box only protein 29	lo-to-hi-hi
65	415743	AA167664	Hs.14333	ESTs, Weakly similar to Z195_HUMAN ZINC	lo-to-hi-hi
	431607	AD003097	Hs.163669	KIAA1271 protein	lo-to-hi-hi
	411978	X06134	Hs.72864	retinol-binding protein 5	lo-to-hi-hi
	453620	BE396163	Hs.125005	ESTs, Weakly similar to ALU5_HUMAN ALU S	lo-to-hi-hi
	431099	Y13367	Hs.249235	phosphoinositide-3-kinase, class 2, alpha	lo-to-hi-hi
70	421687	AL035305	Hs.106823	hypothetical protein MGC14757	lo-to-hi-hi
	439555	AF065560	Hs.145699	ESTs	lo-to-hi-hi
	442349	W40516	Hs.132355	Homo sapiens cDNA: FLJ22119 fis, clone H	lo-to-hi-hi
	410096	AW245200	Hs.267400	hypothetical protein MGC5540	lo-to-hi-hi
	429447	AW812462	Hs.83286	ESTs, Weakly similar to S14747 sphingomy	lo-to-hi-hi
	431602	AL153570	Hs.270571	Homo sapiens mRNA; cDNA DKF2p434L201 (fr	lo-to-hi-hi
75	441715	AB024653	Hs.342655	Homo sapiens cDNA FLJ15229 fis, clone CV	lo-to-hi-hi
	468230	BE311851	Hs.6039	KIAA1624 protein	lo-to-hi-hi
	428788	AF082283	Hs.193616	B-cell CLL/lymphoma 10	lo-to-hi-hi
	450618	AT105873	Hs.142827	P311 protein	lo-to-hi-hi
80	419575	AK006030	Hs.91287	hypothetical protein FLJ11198	lo-to-hi-hi
	404041	AF150993		Homo sapiens endogenous retrovirus RAN1	lo-to-hi-hi
	427004	A921573	Hs.213107	ESTs	lo-to-hi-hi
	401178	AA046772		RNA binding motif protein, X chromosome	lo-to-hi-hi

WO 02/098358

PCT/US02/17594

5	423749	U09848	Ha.132390	zinc finger protein 35 (KIX 18)	to-to-to-to
	428898	AE033070	Ha.194408	KIAA1244 protein	to-to-to-to
	458258	AW006546	Ha.127971	ESTs	to-to-to-to
	429621	BE048708	Ha.50949	ESTs	to-to-to-to
	402185			Target Exon	to-to-to-to
10	415861	H10983	Ha.155919	ESTs	to-to-to-to
	457265	AB023212	Ha.225967	KIAA0935 protein	to-to-to-to
	412419	AW948630		gb:QV0-F10001-050500-226-g05 FT0001 Homo	to-to-to-to
	438397	AA066478	Ha.123206	ESTs	to-to-to-to
	440509	BE101152	Ha.134202	ESTs, Weakly similar to T17299 hypothesis	to-to-to-to
15	423895	AA332215		gb:EST138124 Embryo, 8 week 1 Homo sapiens	to-to-to-to
	400251			NM_004651* Homo sapiens ubiquitin specif	to-to-to-to
	448094	AW296163	Ha.147296	ESTs	to-to-to-to
	432323	AW001409	Ha.274356	hypothetical protein FLJ10547	to-to-to-to
	444290	AA262496		gb:zs0111.r1 NCL_GCAP_GCB1 Homo sapiens	to-to-to-to
20	438903	Z44194	Ha.4994	transducer of ERBB2, 2	to-to-to-to
	438905	N01273	Ha.42380	ESTs	to-to-to-to
	401849			Target Exon	to-to-to-to
	402249			C150005537.g12741444/rupVP_00888.2	to-to-to-to
	406180	AB018249		small inducible cytokine subfamily A (Cy	to-to-to-to
25	443176	A1672546	Ha.170507	ESTs	to-to-to-to
	409259	AW608930	Ha.52184	hypothetical protein FLJ20918	to-to-to-to
	457355	AW969534	Ha.303303	ESTs	to-to-to-to
	452444	BE144022		gb:MR0-HT0166-191199-004-05 HT0166 Homo	to-to-to-to
	406429			Target Exon	to-to-to-to
30	430103	AA465259		gb:aa3203.r1 NCL_GCAP_GCB1 Homo sapiens	to-to-to-to
	439944	AA556757	Ha.124623	ESTs	to-to-to-to
	411283	AW52754		gb:PM1-CT0247-180109-009-c05 CT0247 Homo	to-to-to-to
	458195	R10085	Ha.130370	ESTs	to-to-to-to
	452654	BE004783		gb:MR2-BN0114-270400-004-e11 BN0114 Homo	to-to-to-to
35	425684	AF000589	Ha.159201	Thymosin, beta 4, Y chromosome	to-to-to-to
	429452	A349486	Ha.133958	Homo sapiens cDNA FLJ13202.1s, clone NT	to-to-to-to
	431709	AF220185	Ha.287923	non-acetylated tubulin-associated protein HTO	to-to-to-to
	411701	BE181659		gb:QV1-HT0638-070500-131-g07 HT0638 Homo	to-to-to-to
	430729	A1672560	Ha.301283	KIAA0793 gene product	to-to-to-to
40	447476	BE293496	Ha.20880	ESTs, Weakly similar to 138022 hypothesis	to-to-to-to
	459436	AW293961	Ha.131687	ESTs	to-to-to-to
	405365			CX001212.g17861332/ghAA7F0445.1 (AF2	to-to-to-to
	419555	AA244416		g1m027411.s1 NCL_GCAP_P1 Homo sapiens	to-to-to-to
	448103	U09918	Ha.13804	hypothetical protein dH482023.2	to-to-to-to
45	400595			NM_001085* Homo sapiens hypothetical pro	to-to-to-to
	424154	BE245833	Ha.189854	gb:TCDAPE151938 Pediatric pro-B cell acut	to-to-to-to
	400210			Eos Control	to-to-to-to
	400234			NM_006338 Homo sapiens high density lipo	to-to-to-to
	406235			NM_006338 Homo sapiens high density lipo	to-to-to-to
50	405387			NM_022170* Homo sapiens Williams-Beuren	to-to-to-to
	433075	NM_002395		sorbin 1	to-to-to-to
	406302			C16000022.g17499103/pirIT20903 hypothe	to-to-to-to
	428181	AA423976		gb:zv62h06.s1 Soares_testis_NHT Homo sap	to-to-to-to
	456522	AW851565	Ha.273789	thalassaemia, beta 3	to-to-to-to
55	429940	AA339537	Ha.98347	ESTs, Weakly similar to JC3309 leuka-sap	to-to-to-to
	433565	AA339902	Ha.146211	Homo sapiens HERC2P7 pseudogene, partial	to-to-to-to
	421431	AA650117	Ha.283107	ESTs	to-to-to-to
	448631	A554923		gb:h63h12.s1 Soares_NFL_T1_GBC_S1 Homo s	to-to-to-to
	433521	T66087	Ha.112482	Homo sapiens unknown mRNA sequence	to-to-to-to
60	407187	AA446971		gb:zv65f11.s1 Soares_testis_Islet_Nc2Hf8	to-to-to-to
	450739	A732707	Ha.116506	ESTs, Weakly similar to ALU7_HUMAN ALU S	to-to-to-to
	440004	BE397117	Ha.120824	hypothetical protein FLJ21845	to-to-to-to
	402947	NM_006682		piadin 3 (T isoform)	to-to-to-to
	405529	AW410458		chromosome 11 open reading frame2	to-to-to-to
65	402163			C19001079.g1456717/ghAA223607.1JAC00	to-to-to-to
	404663			ENSP00000251884 NAA1521 protein (Fragme	to-to-to-to
	400220			Eos Control	to-to-to-to
	401444			Target Exon	to-to-to-to
	456824	BE143703		gb:MR0-HT0164-191199-004-03 HT0164 Homo	to-to-to-to
70	400206			Eos Control	to-to-to-to
	458659	AW748656	Ha.332520	Homo sapiens mRNA; cDNA DKF-Zp634A1014 (f	to-to-to-to
	428666	AL080190	Ha.183242	Homo sapiens cDNA, cDNA DKF-Zp634A2022 (f	to-to-to-to
	429442	AA429638	Ha.98606	ESTs	to-to-to-to
	440151	AA868167		gb:ak36a07.s1 Soares_testis_NHT Homo sap	to-to-to-to
75	431046	AW854382	Ha.249126	Homo sapiens clone 24804 mRNA sequence	to-to-to-to
	423914	U0991173	Ha.222362	ESTs, Weakly similar to p40 [H.sapiens]	to-to-to-to
	402469			Target Exon	to-to-to-to
	418155	RA5481	Ha.23719	ESTs, Weakly similar to 138022 hypothesis	to-to-to-to
	448893	A1610818	Ha.7110	ESTs	to-to-to-to
80	422336	AW340568	Ha.7672	ESTs	to-to-to-to
	421290	NM_014358	Ha.103137	LIM homeobox protein 6	to-to-to-to
	450314	AA397540	Ha.60293	Homo sapiens clone 122452 unknown mRNA	to-to-to-to
	402347			Target Exon	to-to-to-to
	415184	AA380436	Ha.211973	homolog of Yeast RRP4 (ribosomal RNA pro	to-to-to-to
	415632	U67085	Ha.78524	Tcd37 homology	to-to-to-to
	423718	AL119520	Ha.180737	Homo sapiens clone 23664 and 23905 mRNA	to-to-to-to

WO 02/098358

PCT/US02/17594

	440140	AVD13840	Hs.202092	ESTs	to-to-to-to
	437241	AA469790	Hs.36568	ESTs	to-to-to-to
	416631	H69466		ghy8B07.r1 Scores fetal liver spleen	to-to-to-to
	424168	L29277	Hs.321677	signal transducer and activator of trans	to-to-to-to
5	401600	BE247275		US snRNP-specific protein, 116 kD	to-to-to-to
	422369	AF023562	Hs.147916	DEAD(R) (Arg-Glu-Ala-Arg) box polysep	to-to-to-to
	414111	BE047679	Hs.152582	hypothetical protein FLJ13117	to-to-to-to
	417138	AA183646	Hs.65771	Homo sapiens chromosome 19, BAC CT-HSPC	to-to-to-to
10	424316	AA447615	Hs.172723	ESTs	to-to-to-to
	458563	BE154075		gb:FMG-HT0339-200400 010-E06 HT0339 Homo	to-to-to-to
	451450	H39556	Hs.32854	ESTs	to-to-to-to
	457015	AA688058	Hs.261544	ESTs	to-to-to-to
	403654			NM_003071:Homo sapiens SWI/SNF related,	to-to-to-to
	435203	AV567127	Hs.264027	ESTs	to-to-to-to
15	405322	BE061159	Hs.22867	ESTs, Moderately similar to unnamed prot	to-to-to-to
	437764	AA767795	Hs.166832	ESTs	to-to-to-to
	432542	AW083620	Hs.16098	claudin 2	to-to-to-to
	436125	AA765895	Hs.162695	ESTs	to-to-to-to
	403217	AL134876		ribosomal protein, large P2	to-to-to-to
20	454023	AL277853	Hs.146141	ESTs	to-to-to-to
	442419	AT149693	Hs.270532	ESTs, Weakly similar to 138022 hypothetical	to-to-to-to
	434587	AT129066	Hs.135457	ESTs	to-to-to-to
	451445	AA017609		gb:z37601.r1 Scores ratine N2b4/R Homo	to-to-to-to
25	447475	BE102229		gb:ZV4.HTD113.090200 452-e12 HTD113 Homo	to-to-to-to
	411053	AW515061		gb:CMG-STC209-271059-062-d10 STC209 Homo	to-to-to-to
	436312	AJ243396	Hs.4565	voltage-gated sodium channel beta-3 subu	to-to-to-to
	450675	AK000724	Hs.201553	karyopherin alpha 5 (importin alpha 7)	to-to-to-to
	451180	Hs.16159	Hs.171937	oligodendrocyte-specific	to-to-to-to
30	427327	AW501456	Hs.288283	Homo sapiens cDNA: FLJ22385 fls, clone H	to-to-to-to
	444521	AW204210	Hs.122275	Homo sapiens mRNA: cDNA DKFZP664N1623 (f	to-to-to-to
	405109	NA7812		CSH-35 protein	to-to-to-to
	450182	AT764400	Hs.240767	Human DNA sequence from clone RP1-12G14	to-to-to-to
	424990	AJUT6596	Hs.154095	zinc finger protein 143 (clone pIZ-1)	to-to-to-to
	428597	AF086361	Hs.194718	zinc finger protein 265	to-to-to-to
35	402602			NM_021186*:Homo sapiens zona pellucida g	to-to-to-to
	426772	AS24039	Hs.192524	ESTs	to-to-to-to
	423759	AT142358	Hs.194361	ESTs, Moderately similar to ALU7_HUMAN A	to-to-to-to
	434550	ALC42940	Hs.63872	KIAA1682 protein	to-to-to-to
	442274	AT733464	Hs.129162	ESTs	to-to-to-to
40	442884	AT076570	Hs.134053	ESTs	to-to-to-to
	400461			Target Exon	to-to-to-to
	407263	T51008		gb:z55606.s1 Stratagene ovary (937217)	to-to-to-to
	408859	AW291672	Hs.258981	ESTs	to-to-to-to
	455615	BE045344	Hs.274523	ESTs, Moderately similar to unnamed prot	to-to-to-to
45	427315	AA179948	Hs.175563	Homo sapiens mRNA: cDNA DKFZP664N763 (f	to-to-to-to
	445375	R07114	Hs.271224	ESTs	to-to-to-to
	419637	AB040569	Hs.93836	DKFZP434N014 protein	to-to-to-to
	422231	AA443512	Hs.101383	ESTs	to-to-to-to
50	437210	AA311443	Hs.263563	Homo sapiens mRNA: cDNA DKFZP68E2317 (f	to-to-to-to
	416038	AA254595		gb:z34032.x1 NCL_GCAP_Fy3 Homo sapiens	to-to-to-to
	448488	NS8790	Hs.258820	ESTs	to-to-to-to
	407549	VY21874	Hs.247057	ESTs, Weakly similar to 2106260A B cell	to-to-to-to
	440296	D30629	Hs.180510	splicing factor proline/glutamine rich (to-to-to-to
	422280	AA315953	Hs.105464	regenerating gene type IV	to-to-to-to
55	434684	AA612445	Hs.287467	Homo sapiens cDNA FLJ11948 fls, clone HE	to-to-to-to
	412657	AV567155		gb:EST388274 MAGC resequences, MAGN Homo	to-to-to-to
	405188			Target Exon	to-to-to-to
	416954	AJ222368		gb:zh04612.x1 Scores NFIL_T_GBC_S1 Homo s	to-to-to-to
60	423700	AA223375	Hs.58605	SV40N upstream reading frame	to-to-to-to
	430265	BE354643	Hs.138004	hypothetical protein FLJ45023.2	to-to-to-to
	436164	T67162	Hs.135127	ESTs, Weakly similar to unnamed protein	to-to-to-to
	431475	AS57669	Hs.40342	putative nuclear protein	to-to-to-to
	445239	AT217375	Hs.170023	ESTs, Weakly similar to CAC30_HUMAN COLLA	to-to-to-to
	430151	AK000501	Hs.339471	Homo sapiens cDNA FLJ22094 fls, clone CD	to-to-to-to
65	448489	AS52875		gb:z57404.x1 NCL_GCAP_CL11 Homo sapiens	to-to-to-to
	424470	BE244261	Hs.325602	Homo sapiens cDNA FLJ23535 fls, clone L	to-to-to-to
	434733	AJ334367	Hs.156357	ESTs	to-to-to-to
	405469	AV571236	Hs.335762	ESTs	to-to-to-to
	414534	U85777	Hs.335665	early development regulator 1 (homolog o	to-to-to-to
70	420382	AV556165	Hs.270034	Homo sapiens, Similar to nuclear localiz	to-to-to-to
	430453	AA476883	Hs.273766	ESTs	to-to-to-to
	435351	T60177	Hs.110054	similar to rat nuclear ubiquitin casein	to-to-to-to
	403218	AL134878		ribosomal protein, large P2	to-to-to-to
75	429678	AV553268	Hs.35390	TIS-associated serine-arginine protein 2	to-to-to-to
	445906	AV555234		ESTs, Moderately similar to PC4255 feni	to-to-to-to
	426633	AA765596	Hs.187651	ESTs	to-to-to-to
	418602	AA250950	Hs.154334	ESTs	to-to-to-to
	425165	N28522		gb:z322 Human ratine cDNA randomly prime	to-to-to-to
	417314	N68168		gb:zaf1c01.s1 Scores fetal liver spleen	to-to-to-to
80	426290	AB52955	Hs.183478	Homo sapiens clone 25081 mRNA sequence	to-to-to-to
	422128	AV561145		gb:CBG-CTCC33-010405-182-a07 OT0033 Homo	to-to-to-to
	432014	H66741	Hs.38540	ESTs, Weakly similar to ALU4_HUMAN ALU S	to-to-to-to

WO 02/09838

PCT/US02/17594

407351	AW383165		gltP3A-HT0344-151299-004-07 HT0344 Homo	to-to-to
443231	W87548	Hs.132932	ESTs	to-to-to
444001	A065087	Hs.152299	ESTs, Moderately similar to S65657 alpha	to-to-to
435064	T70740	Hs.31433	ESTs	to-to-to
435173	AW259545	Hs.235451	ESTs	to-to-to
411831	AW994394		gltRCS-BN0036-060400-014-h12 BN0036 Homo	to-to-to
446572	AW659151	Hs.282961	ESTs	to-to-to
428114	A821548	Hs.98363	ESTs, Weakly similar to I30022 hypothetical	to-to-to
406207			Target Exon	to-to-to
405911			Target Exon	to-to-to
409451	AF012626	Hs.54472	tsaqlu X mental retardation 2	to-to-to
411233	AW833793		gb:QV4-TT006-130106-080-s06 TT0006 Homo	to-to-to
455729	BE072092	Hs.238958	gltP3A-HT0532-160200-003-b11 BT0532 Homo	to-to-to
434954	A4450120	Hs.143942	ESTs	to-to-to
449124	A896403	Hs.143942	ESTs	to-to-to
410324	AW292539	Hs.30177	ESTs	to-to-to
449548	AW789392	Hs.200215	ESTs	to-to-to
418999	AW195747	Hs.21122	hypothetical protein FLJ11830 similar to	to-to-to
414552	AJ133865	Hs.164478	hypothetical protein FLJ21939 similar to	to-to-to
444647	H14718	Hs.11506	Human clone 23589 mRNA sequence	to-to-to
418271	NM_000919	Hs.83920	peptidylglycine alpha-amidating monooxygenase	to-to-to
407939	W05608	Hs.312679	ESTs, Weakly similar to A45019 dymin ho	to-to-to
432876	A167366		gltZ35Df1.x1 Soames_basils_NHT Homo sap	to-to-to
415156	X24908	Hs.78060	phosphatase kinase, beta	to-to-to
432679	A146956	Hs.146723	ESTs, Weakly similar to A55950 transcrip-	to-to-to
412121	A0033061	Hs.73287	KAA1235 protein	to-to-to
418858	AW961605	Hs.21145	hypothetical protein RG083M05.2	to-to-to
423204	Yk_002428	Hs.1861	membrane protein, palmitoylated 1 (SMD)	to-to-to
418348	A157187	Hs.95322	hypothetical protein FLJ23560	to-to-to
410765	A694972	Hs.66180	nucleosome assembly protein 1-like 2	to-to-to
445594	AW054483	Hs.12940	zinc-fingers and homeoboxes 1	to-to-to
415603	H65502	Hs.269853	ESTs	to-to-to
426167	AF039023	Hs.167490	RAN binding protein 6	to-to-to
451752	A5032997	Hs.26966	KAA1171 protein	to-to-to
447124	AW976438	Hs.17428	RBP1-like protein	to-to-to
419872	A422851	Hs.146162	ESTs	to-to-to
447161	A1035316		gltz43b08.x1 Scarsa_total_fetus_Hb2HF3_	to-to-to
445391	T92576	Hs.191168	ESTs	to-to-to
443801	AW205942	Hs.253594	intron of trichothiocephalargel syndro	to-to-to
448708	AW807831	Hs.190488	Homo sapiens, Similar to nuclear localiz	to-to-to
426172	U05567	Hs.163225	zinc finger protein 136 (clone p1Z-26)	to-to-to
421021	A4430018	Hs.109302	ESTs	to-to-to
431749	AL049283	Hs.306292	Homo sapiens mRNA; cDNA DKFZp564F133 (fr	to-to-to
423784	AK000039	Hs.132826	Homo sapiens cDNA FLJ14193 fs, clone PL	to-to-to
419479	A288348	Hs.23450	mitochondrial ribosomal protein S25	to-to-to
450900	H61005	Hs.37302	ESTs	to-to-to
423396	A382555	Hs.127950	brachionin-containing 1	to-to-to
426137	AL040683	Hs.167031	DKFZP566D133 protein	to-to-to
442012	A733277	Hs.128321	ESTs	to-to-to
452271	A4255976	Hs.34599	ESTs	to-to-to
414682	Q79994	Hs.77346	Homo sapiens cDNA; FLJ21983 fs, clone H	to-to-to
432195	A1243669	Hs.8127	KAA0144 gene product	to-to-to
430217	N47863	Hs.180450	ribosomal protein S24	to-to-to
429567	R35506	Hs.328600	Human EST clone S125 marker transposon	to-to-to
438810	AW971448	Hs.43421	hypothetical protein DKFZp761M9121	to-to-to
436796	BE151260	Hs.5320	hypothetical protein	to-to-to
428352	N72324	Hs.55098	ESTs	to-to-to
415308	R05251		gltHSC04H101 normalized infant brain cDN	to-to-to
420146	U34427	Hs.95361	myosin VIIA (Jber syndrome 1B (autosom	to-to-to
434442	AA137415	Hs.132828	ESTs	to-to-to
449429	AA054224	Hs.59847	ESTs	to-to-to
410245	C17908	Hs.194125	ESTs	to-to-to
421169	AF192277	Hs.330780	cytochrome P450, subfamily IIB (phenobar	to-to-to
438237	R11528	Hs.271959	ESTs	to-to-to
440668	A895338	Hs.191074	ESTs	to-to-to
422068	A807519	Hs.104520	Homo sapiens cDNA FLJ13694 fs, clone PL	to-to-to
410216	BE061839		gltR1C1-B10254-290100-015-s06 B10254 Homo	to-to-to
438437	A207788	Hs.343628	seryltransferase 4B (beta-galactosidase	to-to-to
417061	A875944	Hs.188691	Homo sapiens cDNA FLJ12033 fs, clone HE	to-to-to
403046			NM_005659 Homo sapiens transmembrane pr	to-to-to
404528	A912555		peptide YY, 2 (serpinaphosin)	to-to-to
438734	AC055013	Hs.149	cAMP response element-binding protein CR	to-to-to
432991	N64777	Hs.44666	ESTs	to-to-to
403745			ENSP00000225812-XGAA1494 protein (Fragm	to-to-to
411448	AA178955	Hs.271439	ESTs, Weakly similar to I30022 hypothetical	to-to-to
422480	AW445014	Hs.197746	ESTs	to-to-to
404555			Target Exon	to-to-to
436184	BE154067	Hs.139960	ESTs, Weakly similar to ZNF11 HUMAN ZINC	to-to-to
427702	N76589	Hs.14454	ESTs, Weakly similar to TFIRD subunit TA	to-to-to
440695	AW088363	Hs.246240	ESTs	to-to-to
424881	AL119980	Hs.153618	HCGVIIb-1 protein	to-to-to
440573	BE550891	Hs.270924	ESTs	to-to-to

PCT/US02/17594

[illegible]

WO 02/098358

PCT/US02/17594

	414483	R25513	Hs.10683	ESTs	hi-hi-to
	451273	NM_014811	Hs.26163	KIAA0649 gene product	hi-hi-to
	437052	AA861697	Hs.120591	ESTs	hi-hi-to
5	440049	R66699	Hs.19769	hypothetical protein MGC4174	hi-hi-to
	429483	AA974832	Hs.128768	ESTs	hi-hi-to
	411265	BE267307	Hs.10114	growth suppressor 1	hi-hi-to
	425188	A0002052	Hs.155071	hypothetical protein FLJ11190	hi-hi-to
	436315	BE390513	Hs.27355	hypothetical protein MGC4837	hi-hi-to
10	402327	A127076	Hs.306201	hypothetical protein DNFZp56403/278	hi-hi-to
	431989	BE641395	Hs.10114	ESTs, Weakly similar to unknown protein	hi-hi-to
	418824	AW751661	Hs.53542	chromosomethylosis gene; KIAA0595 prot	hi-hi-to
	449226	AB002365	Hs.23311	KIAA0367 protein	hi-hi-to
	450149	AW999781	Hs.132853	Zfc family member 2 (odd-paired Drosoph	hi-hi-to
	418445	NM_035239	Hs.85146	vells avian erythroblastosis virus E26 o	hi-hi-to
15	458602	BE449905	Hs.231754	ESTs	hi-hi-to
	410102	AW248508	Hs.279727	ESTs; homologue of PEM-3 [Clona savignyi]	hi-hi-to
	451062	AL110125	Hs.25910	Homo sapiens mRNA; cDNA DNFZp56403/278	hi-hi-to
	407633	NM_007008	Hs.37189	similar to rat HREVI107	hi-hi-to
	418941	AJ462370	Hs.239527	ETD-50Dw-associated protein 5	hi-hi-to
20	407059	X06404		gh4-sapiens cyclin E gene.	hi-hi-to
	456956	BE162704		gp.PM1-HT0454-301299-001.d8 HT0454 Homo	hi-hi-to
	437763	AA469369	Hs.5831	tissue inhibitor of metalloproteinase 1	hi-hi-to
	451404	AA460775	Hs.5295	ESTs, Weakly similar to T17248 hypotheti	hi-hi-to
	423494	AJ233439	Hs.184634	hypothetical protein FLJ20005	hi-hi-to
25	414967	D61283	Hs.45206	ESTs	hi-hi-to
	456415	AT34051	Hs.277102	ESTs, Weakly similar to ALU1_HUMAN ALU S	hi-hi-to
	400183			Eos Control	hi-hi-to
	400188			ENSP0000024402;CCNA FLJ11691 fls, abn	hi-hi-to
	403893			ENSP0000023705P;Prothocadherin alpha 6 p	hi-hi-to
30	423809	AJ223833	Hs.154483	ESTs	hi-hi-to
	400170			Eos Control	hi-hi-to
	403291			Target Exon	hi-hi-to
	422026	U80736	Hs.110826	riminotide repeat containing 9	hi-hi-to
	417130	AWZ76858	Hs.81256	S100 calcium-binding protein A4 (calcium	hi-hi-to
35	432472	AA548781	Hs.136418	ESTs	hi-hi-to
	406231			CD201066g[1025742s]ref[NP_033892.1] CD	hi-hi-to
	400141			Eos Control	hi-hi-to
	428971	BE278404	Hs.285813	hypothetical protein FLJ11807	hi-hi-to
	422390	AW450893	Hs.121830	ESTs, Weakly similar to T42582 hypotheti	hi-hi-to
40	425538	BE270918	Hs.184026	Homo sapiens, clone IMAGE:534875, mRNA,	hi-hi-to
	456972	A054347	Hs.2017	ribosomal protein L28	hi-hi-to
	459522	A226949	Hs.107740	Yoppel-like factor 2 (Ygf)	hi-hi-to
	418615	A068453	Hs.19487	ESTs, Weakly similar to CNH_HUMAN CORNI	hi-hi-to
	448439	BE513082	Hs.28229	ARG99 protein	hi-hi-to
45	445416	AW159377	Hs.127179	cryptic gene	hi-hi-to
	402359	Z33024		Rho GTPase activating protein 1	hi-hi-to
	402675	Z23024		Rho GTPase activating protein 1	hi-hi-to
	408611	AA807544		ESTs, Weakly similar to B34323 GTP-bindi	hi-hi-to
	446527	A973016	Hs.15725	hypothetical protein SB848	hi-hi-to
50	400247			Eos Control	hi-hi-to
	430289	A0007952	Hs.238039	hypothetical protein FLJ11090	hi-hi-to
	400133			Eos Control	hi-hi-to
	418816	T29621	Hs.88778	carboxyl reductase 1	hi-hi-to
	433579	BE264473	Hs.284297	hypothetical protein from EUROIMAGE 1967	hi-hi-to
55	401952			Target Exon	hi-hi-to
	410349	AW863021	Hs.323445	ESTs, Weakly similar to T203_HUMAN TRANS	hi-hi-to
	417558	AF045229	Hs.82280	regulator of G-protein signalling 10	hi-hi-to
	446861	AW007332	Hs.10450	Homo sapiens cDNA: FLJ22063 fls, clone H	hi-hi-to
60	404489			Target Exon	hi-hi-to
	408802			Target Exon	hi-hi-to
	456206	L29073	Hs.198726	cold shock domain protein A	hi-hi-to
	457133	M54958		v-H-ras2 Kirsten rat sarcoma 2 viral on	hi-hi-to
	455330	C16851		gbc16931 Clontech human avian polyA mRN	hi-hi-to
	433041	BE258468	Hs.289080	colon cancer-associated protein Mcl1	hi-hi-to
65	446455	AA31798	Hs.164192	ESTs, Weakly similar to Y161_HUMAN HYPOT	hi-hi-to
	414911	NM_000107	Hs.77802	damago-specific DNA binding protein 2 (4	hi-hi-to
	414882	AL021154	Hs.76884	inhibitor of DNA binding 3, dominant neg	hi-hi-to
	422311	A0703515	Hs.114948	cytokine receptor-like factor 1	hi-hi-to
70	447329	BE090617		ESTs, Moderately similar to ALLU_HUMAN A	hi-hi-to
	412942	AL120344	Hs.75074	mitogen-activated protein kinase activat	hi-hi-to
	407047	BE284407	Hs.99910	phosphotuckinase, platelet	hi-hi-to
	431912	A060552	Hs.76549	ESTs, Weakly similar to A06154 AMI subst	hi-hi-to
	445606	AT121118	Hs.15159	chemokine-like factor, alternatively sp	hi-hi-to
75	408633	AW953372	Hs.46577	PRC200 protein	hi-hi-to
	433676	AW977653	Hs.75319	ribonucleotide reductase M2 polypeptide	hi-hi-to
	424660	AA158727	Hs.150555	protein predicted by clone 23733	hi-hi-to
	426234	AW152225	Hs.165509	ESTs, Weakly similar to D8222 hypotheti	hi-hi-to
	439819	AJ205079	Hs.5693	hypothetical protein FLJ20420	hi-hi-to
80	410174	AJ305007	Hs.59461	DNFZP434C245 protein	hi-hi-to
	410442	X73424	Hs.63378	prokaryotic Coenzyme A carboxylase, beta p	hi-hi-to
	429190	H18650	Hs.92602	ESTs	hi-hi-to
	423619	T48691	Hs.249159	adrenomedullin, alpha-2/-, receptor	hi-hi-to

WO 02/098358

PCT/US02/17594

433764	AW753675	Hs.39962	ESTs	hi-to-hi
421998	R74441	Hs.117175	poly(A) ₁ binding protein, nuclear 1	hi-to-hi
451593	AF151879	Hs.25706	C3-121 protein	hi-to-hi
452092	BE245374	Hs.27842	hypothetical protein FLJ11210	hi-to-hi
447425	A963747	Hs.18573	acylphosphatase 1, erythrocyte (common)	hi-to-hi
421554	AW153287	Hs.109469	suppressor of var1 (Scorv1a) 3 like	hi-to-hi
432502	NM_014641	Hs.277585	KSA0170 gene product	hi-to-hi
429597	NM_003816	Hs.2442	a diintegrin and metalloproteinase domain	hi-to-hi
434203	BE262677	Hs.283558	hypothetical protein PRO1855	hi-to-hi
433481	AW075485	Hs.280449	phosphoserine aminotransferase	hi-to-hi
409142	AL136877	Hs.50138	SAC4 (structural maintenance of chromosome	hi-to-hi
436574	AA69798	Hs.165190	ESTs	hi-to-hi
438182	AW342140	Hs.182545	ESTs, Weakly similar to ALU1_HUMAN ALU S	hi-to-hi
449103	T24968	Hs.23038	HSPC071 protein	hi-to-hi
421085	A054133	Hs.30212	thyroid receptor interacting protein 15	hi-to-hi
446539	AL133353	Hs.16506	C3-32 protein	hi-to-hi
408570	NM_003542	Hs.46423	Hi histone family, member G	hi-to-hi
410073	AW408153	Hs.58458	catenin (cadherin-associated protein), a	hi-to-hi
450912	AW539251	Hs.25547	v-fes FBJ murine osteosarcoma viral onc	hi-to-hi
434701	AA460478	Hs.321707	KIA02742 protein	hi-to-hi
450455	AL117424	Hs.25035	chloride intracellular channel 4	hi-to-hi
451144	AW656103	Hs.51712	pyruvate dehydrogenase kinase, isozyme	hi-to-hi
427390	A432153	Hs.282321	Home sapiens cDNA: FLJ23111 fn3, clone L	hi-to-hi
451831	NM_001874	Hs.460	activating transcription factor 3	hi-to-hi
406775	T16206	Hs.237154	ESTs, Highly similar to LKH1_HUMAN L-LAC	hi-to-hi
428157	A738719	Hs.198427	hexokinase 2	hi-to-hi
408096	BE250152	Hs.83755	dihydrofolate reductase	hi-to-hi
418203	K54842	Hs.83758	CDC28 protein kinase 2	hi-to-hi
443338	H71444	Hs.301	adenomodulin	hi-to-hi
422082	AA013188	Hs.111244	hypothetical protein	hi-to-hi
407907	A752235	Hs.41270	procollagen-lysin, 2-oxoglutarate 5-dio	hi-to-hi
419355	AW598813	Hs.79428	BCL2/adrenomedullin E1B 19kD-interacting pro	hi-to-hi
415551	AW582258	Hs.91011	anterior gradient 2 (Xenopus laevis)	hi-to-hi
434094	AA305599	Hs.238005	hypothetical protein PRO2013	hi-to-hi
443961	F13272	Hs.111334	ferritin, light polypeptide	hi-to-hi
422975	AA347720	Hs.122659	KIA0264 protein	hi-to-hi
403314	AA339501	Hs.237138	pro-B-cell colony enhancing factor	hi-to-hi
412804	AA421404	Hs.345689	nuclear protein p40; homolog of yeast	hi-to-hi
408089	H69799	Hs.42644	thionin-like	hi-to-hi
406890	W45393	Hs.55888	activating transcription factor 7	hi-to-hi
422332	A0583251	Hs.8248	target CAT	hi-to-hi
403385	AF091086	Hs.44563	hypothetical protein	hi-to-hi
441252	AW390501	Hs.183047	hypothetical protein MGCA359	hi-to-hi
433089	X76732	Hs.3184	nucleobindin 2	hi-to-hi
443837	A384625	Hs.5884	sphincter pole body protein	hi-to-hi
429108	AA222037	Hs.185458	programmed cell death 5	hi-to-hi
441181	AA165525	Hs.121078	peptidylprolyl isomerase (cyclophilin)-1	hi-to-hi
447397	BE247676	Hs.18442	E-1 enzyme	hi-to-hi
427505	AA301582	Hs.178781	26S proteasome-associated pept1 homolog	hi-to-hi
430287	AW182459	Hs.125759	ESTs, Weakly similar to LEL5_HUMAN LEUKE	hi-to-hi
415857	A085115	Hs.127197	Home sapiens cDNA: FLJ11361 fn3, clone HE	hi-to-hi
423198	NM1933	Hs.1034	cell division cycle 25A	hi-to-hi
407687	AK002011	Hs.37558	hypothetical protein FLJ11149	hi-to-hi
431374	BE258532	Hs.251871	CTP synthase	hi-to-hi
413273	U75719	Hs.75267	stem-loop (histone) binding protein	hi-to-hi
427799	A064739	Hs.58606	ESTs	hi-to-hi
443881	R64612	Hs.237146	hypothetical protein FLJ12752	hi-to-hi
415209	AA239775	Hs.79078	MAD2 (mitotic arrest deficient, yeast, h	hi-to-hi
421834	BE543205	Hs.286771	DRP2P556A052 protein	hi-to-hi
411263	BE287602	Hs.65360	kinesin-like 5 (mitotic centromere-asso	hi-to-hi
413924	AL119954	Hs.75215	reladin-1	hi-to-hi
450598	AF151076	Hs.25199	hypothetical protein	hi-to-hi
438453	BE264874	Hs.5566	thyroid hormone receptor interacting 13	hi-to-hi
429612	A0302648	Hs.256587	pituitary tumor-transforming 1	hi-to-hi
443406	AF109158	Hs.5329	chromosome 20 open reading frame 1	hi-to-hi
452363	C18825	Hs.29191	epithelial membrane protein 2	hi-to-hi
419879	Z17805	Hs.53564	Homer, neuronal immediate early gene, 2	hi-to-hi
422363	T59719	Hs.115474	replication factor C (activator 1) 3 (38	hi-to-hi
415095	BE257531	Hs.78956	proliferating cell nuclear antigen	hi-to-hi
424308	AW575531	Hs.154443	mitochondrion maintenance deficient (S	hi-to-hi
447519	U46258	Hs.336665	ESTs	hi-to-hi
437679	NM_014214	Hs.5753	inzeol(myo)-1for (4)-monophosphatase 2	hi-to-hi
445535	A0302563	Hs.15787	clonin (rho-kinase-activating, semaphorin	hi-to-hi
422094	AF129535	Hs.220227	F-box only protein 5	hi-to-hi
440334	BE276112	Hs.7105	zinc finger protein 259	hi-to-hi
421521	H83363	Hs.58520	translocase of inner mitochondrial membr	hi-to-hi
422538	NM_001809	Hs.1594	centromere protein A (17kD)	hi-to-hi
427719	A355122	Hs.134748	ESTs	hi-to-hi
422283	AW411307	Hs.114311	CDC45 (cell division cycle 45, S. cerevis	hi-to-hi
424840	D79987	Hs.153479	extra spindle poles, S. cerevisiae, homo	hi-to-hi
418216	AA652240	Hs.283099	AF15q14 protein	hi-to-hi
412140	AA219591	Hs.73625	RAB8 interacting, kinesin-like (rakibins	hi-to-hi

WO 02/098358

PCT/US02/17594

18322	AA284166	Hs.84113	cyclin-dependent kinase inhibitor 3 (CDK	hi-to-hi
28479	Y00272	Hs.334582	cell division cycle 2, G1 to S and G2 to	hi-to-hi
49722	BE280074	Hs.23960	cyclin B1	hi-to-hi
17933	X02338	Hs.82962	thymidylate synthetase	hi-to-hi
43501	AF217513	Hs.27995	clone H20510 PRO2018p1	hi-to-hi
13943	AW094416	Hs.144687	Homo sapiens cDNA FLJ12981 fls, clone NT	hi-to-hi
424905	NM_002497	Hs.153704	NIMA (pewee in mitosis gene a)-related k	hi-to-hi
427765	AW409701	Hs.15378	baculoviral IAP repeat-containing 5 (sur	hi-to-hi
425397	J04068	Hs.155346	topoisomerase (DNA) I alpha (170Kd)	hi-to-hi
44371	BE020274	Hs.239	lockhead box M1	hi-to-hi
122956	BE545072	Hs.122579	ECT2 protein (Epithelial cell transformi	hi-to-hi
444783	AK001468	Hs.62180	sailline (Drosophila Scaps homolog), act	hi-to-hi
453884	AA355925	Hs.36232	KIAA0186 gene product	hi-to-hi
416980	AA381133	Hs.80664	High-mobility group (nonhistone chromos	hi-to-hi
42432	BE035889	Hs.38178	hypothetical protein FLJ23468	hi-to-hi
417308	H60720	Hs.81892	KIAA0101 gene product	hi-to-hi
433133	AB027249	Hs.104741	PDZ-binding kinase: T-cell originated pr	hi-to-hi
432626	AA471058	Hs.273544	acetyl-Coenzyme A acetyltransferase 2 (a	hi-to-hi
411020	W9283	Hs.35962	ESTs	hi-to-hi
142281	AB10064	Hs.14119	ESTs	hi-to-hi
435602	AF217515	Hs.283532	uncharacterized bone marrow protein BM03	hi-to-hi
404882			Target Exon	hi-to-hi
445269	AW263155	Hs.14559	hypothetical protein FLJ10540	hi-to-hi
17841	AS21559	Hs.7331	hypothetical protein FLJ22116	hi-to-hi
400681			NM_020602:Homo sapiens hypothetical prot	hi-to-hi
19356	AI55166	Hs.7331	hypothetical protein FLJ22116	hi-to-hi
400292	AA025077	Hs.72472	BNP-R18	hi-to-hi
15539	A73381	Hs.72472	BNP-R18	hi-to-hi
453635	AI333770	Hs.42572	ESTs	hi-to-hi
420005	AW271108	Hs.133294	ESTs	hi-to-hi
428450	NM_014791	Hs.184339	KIAA0175 gene product	hi-to-hi
336291	BE588452	Hs.344037	protein regulator of cytokinesis 1	hi-to-hi
411822	BE114410	Hs.23044	RAD51 (S. cerevisiae) homolog (E coli Pa	hi-to-hi
428484	AF104032	Hs.184601	solute carrier family 7 (calcionic amino	hi-to-hi
18526	BE019020	Hs.85838	solute carrier family 16 (monocarboxylic	hi-to-hi
458909	AW125212	Hs.22985	snb-associated polypeptides, 30kD	hi-to-hi
444984	HI1674	Hs.132898	fatty acid desaturase 1	hi-to-hi
447342	AI195268	Hs.193322	Homo sapiens, Similar to RIKEN cDNA 2010	hi-to-hi
428330	L22524	Hs.22556	matrix metalloproteinase 7 (matrilysin,	hi-to-hi
428336	AA203115	Hs.183752	microsomal protein, beta-	hi-to-hi
430389	AB117428	Hs.240846	DIV2/MS4D145 protein	hi-to-hi
177318	AW563597	Hs.240845	ESTs	hi-to-hi
422545	X02781	Hs.287620	flotaxin 1	hi-to-hi
17640	D30857	Hs.82353	protein C receptor, endothelial (EPCR)	hi-to-hi
428209	AK001379	Hs.121028	hypothetical protein FLJ10549	hi-to-hi
425680	L11144	Hs.1907	galactin	hi-to-hi
16836	D54745	Hs.80247	cholecystokinin	hi-to-hi
434170	AA826509	Hs.122329	ESTs	hi-to-hi
427958	AA418000	Hs.95280	potassium intermediate/small conductance	hi-to-hi
450706	AW125227	Hs.59761	ESTs, Weakly similar to DAPI_HUMAN DEATH	hi-to-hi
450089	AW282523	Hs.254110	ESTs	hi-to-hi
414219	W20010	Hs.75823	ALL1-fused gene from chromosome 1q	hi-to-hi
19201	M22324	Hs.12339	stony (membrane) aminopeptidase (aminop	hi-to-hi
426263	AF597774	Hs.257785	carotene palmitoyltransferase 1, liver	hi-to-hi
462246	AF043229	Hs.82260	regulator of G-protein signalling 10	hi-to-hi
456907	AB60190	Hs.106070	cyclin-dependent kinase inhibitor 1C (p5	hi-to-hi
408437	AW557744	Hs.278409	acinar proline rich protein	hi-to-hi
421180	BE410992	Hs.258730	heme-regulated inflation factor 2-alpha	hi-to-hi
415457	BE313164	Hs.75361	gene from NF2/meringliome region of 22q12	hi-to-hi
420415	H6191	Hs.289014	ESTs, Weakly similar to AC3835: ccrn2 p	hi-to-hi
449230	BE613348	Hs.211579	melanoma cell adhesion molecule	hi-to-hi
17979	AU077284	Hs.83081	GTP cyclohydrolase I feedback regulatory	hi-to-hi
421877	AW260380	Hs.106959	mitochondrial ribosomal protein L12	hi-to-hi
142482	AA069930	Hs.334885	mitochondrial GTP binding protein	hi-to-hi
428423	AU076517	Hs.184276	solute carrier family 1 (sodium/hydrogen	hi-to-hi
429447	AA306782	Hs.122552	G-2 and S-phase expressed 1	hi-to-hi
441072	AW075480	Hs.39504	hypothetical protein MGC34308	hi-to-hi
115938	BE383607	Hs.78921	A kinase (PRKA) motor protein 1	hi-to-hi
432278	AL137506	Hs.274256	hypothetical protein FLJ23563	hi-to-hi
446651	AA393907	Hs.97179	ESTs	hi-to-hi
431515	NM_012152	Hs.258583	endothelial differentiation, lysophospha	hi-to-hi
465345	AW003850	Hs.12352	chromosome 1 open reading frame 21	hi-to-hi
459665	AA010319	Hs.60389	ESTs	hi-to-hi
438321	AA576635	Hs.6153	CGL-48 protein	hi-to-hi
16783	AA206186	Hs.79889	monocyte to macrophage differentiation-a	hi-to-hi
453563	AW080908	Hs.181163	hypothetical protein MGC3529	hi-to-hi
432393	AW050693	Hs.133598	hypothetical protein FKSG203	hi-to-hi
433914	AF108138	Hs.112160	Homo sapiens DNA helicase homolog (Pif-1)	hi-to-hi
144907	X90725	Hs.77597	polo (Drosophila)-like kinase	hi-to-hi
432375	BE536069	Hs.2962	S100 calcium-binding protein P	hi-to-hi
440773	AA352702	Hs.37147	Homo sapiens, Similar to RIKEN cDNA 2700	hi-to-hi
145994	NM_002923	Hs.78944	regulator of G-protein signalling 2, 2k.	hi-to-hi

[illegible]

WO 02/098358

PCT/US02/17594

TABLE 2B

Play: Unique Eco probe/identifer number
CAT number: Gene cluster number
Accession: GenBank accession numbers

5	Play	CAT Number	Accession
	406660	107294_1	AA825775 AA056342 A1538978 AW975281 AA664586
	409051	106999_1	AA080912 AA075316 AA083403 AA076584 AA078992 AA084926 AA081881 AA113913 AA113892 AA083621 AA134801 AA082953 AA070343
			AA082636 AA087419 AA085233 AA071282 AA070900 AA082636 AW974306
10	401223	110143_1	AA083403 AA070323 AA070050
	410216	1184664_1	BE061839 AW859633 AW600085
	410451	1204118_1	BE065687 BE065637 AW749002 H73690
	410488	120611_1	AA355749 AA085320 AW966533 AA340319 BE170936
15	411953	1233446_1	AW815361 H71962 AW815377 AW815948 AW815941 AW815947 BE152831 BE152490 BE149043 BE149078 BE149335 BE149067
	411233	1233636_1	AW833793 AW833799 AW833746 AW833271 AW833795 AW833962 AW833667 AW833377
	411283	1237666_1	AW852754 AW852897 AW852757 AW852617 BE172755 AW853444
	411701	1254446_1	BE181659 AW890575 AW850738
	411831	1262400_1	AW894394 AW855000 AW855005 AW855091 AW865814 AW855808
20	412419	1293418_1	AW948630 AW948626 AW948634 AW948616 AW948627 AW948615 AW948631 AW948605 AW948611 AW948610 AW948633 AW948623
			AW948628 AW948604 AW948602 AW948607
	412492	130082_1	AW962604 AA368638 AA112257
	412657	1318507_1	AW976165 CD4030
	413351	1363660_1	BE068618 BE068623 R81218 R69229
25	413509	1374319_1	BE145419 BE145433
	413672	1382512_1	BE165636 BE165630 BE155700 BE166449 BE166653 BE165533 BE165624 BE166670 BE166721 BE166723
	415308	1533675_1	R52521 H13748 Z40208 H14747
	415516	1539185_1	F11411 R15227 Z439151120790
	416508	1597894_1	R38768 T53143 H80012
	416631	1605019_1	H69466 H63884 N58694
30	419954	183427_1	AD222358 H73390 D61648 AA243520 AA190953
	417314	1868548_1	N65168 N65168 N65450
	418056	171841_1	AA524886 AW971547 AA211537
	418259	173388_1	AA215404 AW990909 BE464132 AW271459 H74332 AD202061
35	418574	17690_1	N28754 N28747 A158146 AW979395 AA322671 AW955043 AW950326 AA776406 AA016250 AA843678 H1451682 N23137 N23129
			WY0051 A138748 AA631327 AW95846 AW945895
	419655	185894_1	AA244415 AA244401
	420811	196677_1	AA807744 AA280648 AD23056 AD22744 AW105288 AA829425 AW452095 AW129317 R19033 AA282024
	421911	208987_1	AL041520 AA300086
40	421974	209807_1	AA301270 AA301379 AA301366
	422126	21894_1	AW881145 AA460718 M85327 AA304575 T06067 AA331991
	423208	224602_1	H93846 AA302697 AW954870 BE143880
	423478	22861_1	AL035833 F11754 F11783 H18042 T66089 H28379 R19493 AW134660 AD299437 AL133995 AA057405 H78357 AA917450 AL020862 T09262
45	423686	233006_1	T65008 H25290 AD200874 AA844415 AW732887 AT91786 AT933447 AA888768 N62128 T06261 AW1596336
	424933	241254_1	AA832216 AA403110 AW965299
	425074	246486_1	AA834729 AA433776 AA344370
	425291	249618_1	AA495930 AA470890 H97831 AA330358 BE186712
	425590	258778_1	AA354572 AW062361 AW813419 AW816041 A744849
50	426413	269650_1	AA368951 AA470899 AA469425
	428181	287353_1	AA577823 AW954494 AD22868
	429163	300543_1	AA425975 AA437075 BE036469
	429540	305828_1	AA884788 AW974271 AA929715 AA447312
	430068	312849_1	V85776 AA454536 AA562038 H90189
55	430103	313880_1	AA456964 M85405 AA947505
	430439	31808_1	AA465256 AW897142 AW897144
	431089	327825_1	AL133561 AL041090 AL117481 AL122069 AW938292 A196826
	431843	336324_1	BE041395 AA491826 AA21946 AA715960 AA660102
60	432079	341114_1	AA516420 C14818 C14815 C151667 C15068 D80763 D60656 AW970134 AA543007 D81004 D60184 A1498371 D60362 D60181 C15876
	432340	345248_1	AW872744 AA525233 A165014
	432676	352582_2	AA542422 AA532937 T81234
	433076	35880_1	A187366 AA538869 AA618478
65			NM_002949 X98248 AA233278 AA846376 AA105690 A1470533 BE327147 AW291971 AA071125 A1198417 A1366213 A1684442 A1337018
			AA175049 H85493 AA596895 AA888006 AA415326 AA418378 H71901 ALM3654 AA426301 AA416275 AA423275 A1036861 BE277220 BE367506
			N93711 AW875504 AA418268 AL079651 H88743 AW900219 AW852097 A4684386 T82310 AA074545 AA421725 A856441 A1920966
			AW959348 H52267 BE464032 AA473548 A1369602 BE552306 A199016 AW518351 A1232959 AW950963 AA018353 A1273737 AL042658
			AA411308 AA402810 H30111 AW013881 AW366432 AW752635 AW376124 AD290202 AD292121 AA340647 BE013672 BE409874 AA351915
			BE417028 BE071988 AW402892 AW247466 R95233 AA134761 BE254019 BE265105 D83136 BE313080 BE547713 BE536578 BE546749
			AA234161 H71538 BE253877 H87598 H58972 AA359880 BE076629 BE253957 AA526113 BE252466 AW804459 D33965 R87395 AA091832
			BE055386 AA268222 AA994155
70	434280	382816_1	R76593 AF147390 K76994
	434609	38950_1	A169252 A193343 A1800610 A1577711 F24263 AA61876
	435022	398959_1	AA133549 AA129984 AA084981
	435716	425440_1	A121940 H87106 A1744628 AA083846 AA643417 AA453416 Z70715
	436862	42814_1	BE514383 AA071273 AW427987 AW873286 BE312102 AW748924 BE071985 AW957333 BE071945 BE072005 AW955155 BE071965 AW243821
75	437576	43882_1	BE072000 BE071960 AW957360 AW748930 AW373000 X97303 AW3999522 BE000192 BE062219 BE266655 BE264970
	438869	46951_1	AF375009 R83109 R63068
	438882	46949_1	AA876595 AA833754 AW978946
	438960	467544_1	AW952384 A1982587 AA828822
	439046	468133_1	AA947354 AA829660 A857296
	439848	477806_1	AW979249 DE3277 AA84098
	440151	487109_1	AA868167 F21558 F31416 F36624
80	440507	495677_1	H89394 BE147498

WO 02/098358

PCT/US02/17594

441102 509604_1 AA973925 AI299888 AA917019 H63236 T90771
442048 531432_1 AA874603 AI084316 AW300465
443161 561305_1 AI038316 AI344631 AI261653
444290 59994_1 AA262496 AV648929 AA303535 D61644 D78724
5 444314 606667_1 AI140497 AW738625 AW749626 AW749644
445806 55133_1 AV055234 AW066532 AA402239
447329 71759_1 BE265517 AW070792 AW054490 AW014965 F27436 AA947336 F15843 H89336 AA563626 F17712 BE754679 AA421821 AA284852 AA477751
AW025246
10 447448 722246_1 BE244285 C18429 H42373 AI020706 AI379786 R55439 AIY276142
448150 752165_1 AI472167 AI1950316 R02175
448449 763247_1 AI523875 R47792 R40761
448631 772996_1 AI554923 AI02356
448738 77790_1 BE514061 W011988 AW500790
15 452410 9163_1 AL133619 AA468118 AA363064 AA76447 T09430 AB73759 AA524695 AI581345 AI300620 AW499812 AA256162 AI593724 AI66732 AA602400
AA95453 AI204535 AW195641 AI157468 AA152629 AA338262 AA531072 AV932707 AI435410 AW727464 AI215524 AA627447 R74039
N5051 AI064128 AW513621 AA069351 AA058265 AA63388 AA614641 W61004 AA567060 AI214351 AA730140 AI125754 AI200813 AI208603
AI566582 A1807095 AI176529 AA505900 AI388448 AI686077 AI582930 AW085038 AA757863 AA730154 AW767072 AI4A6316 AI734130 AI734138
AA426284 AA433997 AI741241 AW043563 AI732741 AI732734 AA437369 AA425820 AA664048 R74130
20 BE144022 BE143969 BE143915
BE004783 BE040474 AI911789
BE160229 AWB19879 AW320179 AWB19662 AWB19676 AWB20169 BE153201 AW993736 BE152911
AWB50818 AWB50633 AWB351100
BE148152 BE148133 BE148159 BE148132 AW685107
BE063633 BE063835 BE063866 BE063705 BE063948 BE061416 BE063044
25 BE154075 BE153973 BE0764861 BE153852 BE153647 BE064684 BE153602 BE065075 BE154018 BE065472 BE064642 BE153557 BE153509
BE072092 BE072106 BE072086 BE072093 BE072103
BE143703 BE143631 BE143629 BE143702
BE162704 BE162705 BE162732 BE162702 BE162694
30 R0002 X42921 F06132
N54568 NM D04955 AI808924 AL135130 AN202100 AA476848 AI740448 M17087 K03210 M35505 M35504 L00049 AI180585 W35273 X01669
X02825 V23635 A0554920 A1539465 AA425263 AI469981 W21091 T28976 AW977922 BE550180 AWB64973 AI148839 AA117295 AA811229
AI343510 AI4766141 BE215938 H95249 AA303986 AW504574 AA232870 AI770018 AA262948 AW450239 AW362390 AW060417 AW499941
AI425957 AV303905 AA330647 A4261160 T27396 H63307 A461543 AA556548 AA369410 AWB53656 AW595847 AWB63103 AWB06549
AI567016 W07374 AW474707 AA505384 AA021956 AV0949515 A301729 N33863 AA111821 AA401640 AW539461 AI120706 A500024
AW771391 H46567 D51551 AA330460 R14134 AI301629 N64676 AV059069 AB607660 AI004579 AA239727 AA453082 AW937642 A4676681
AI4737010 AA472481 A4281094 AA564243 BE464958 BE462865 AW167917 F A4843916 AI0525301 AI015987 N25230 AI089491 AW173465
35 H436477 AA749469 BE330651 N41020 AI055915 F00075 AA064878 H26970 AA026939 AW019991 AW796631 AW853262 H48532 BE254662
A264302 A4839246 R40473 H02312 A4548116 A4342730 A424324 R0351 R41589 R4996 AA54442 F01113 AC215686 AA721296 R79383
H46421 R70656 H55554 AA223758 N95349 AI374913 AI306683 AA015509 AA916546 AA53570 AA772321 AI692775 AA195733 A474563
AWB73048 A429133 AI028182 AI374920 AW572807 AA062223 A4383684 T97256 H69136 AA322906 AW1191612 N31974 AI690584 N39418
40 AA634877 AA79469 BE330651 N41020 AI055915 F00075 AA064878 H26970 AA026939 AW019991 AW796631 AW853262 H48532 BE254662
AI1554035 A175481 AW195712 C03289 A0553514 AV580766 AW060435 I070113 C05523 R01694 H9949 AV55836 A555679
H08137 AA364411 AA12584 C02740 W32014 R58168 C05526 BE539017 N24354 AA267391 N60109 F05452 R1274C H08287 AI138354
AW020801 BE173843 BE178018 BE178336 BE178360 BE173107 BE173805 BE178215 BE178186 BE178447 BE178362 BE178422 BE179424
45 BE178043 BE176093 BE178400 BE178356 BE178441 BE178438 BE178467 AI091259 BE177839 BE176094 R28456 BE177844 BE178100
AA262397 R07069 WB9334 W93668 AA296711 BE176141 BE177803 BE178449 AA167718 H08984 BE178017 BE178329 BE177699 BE177936
AA095144 N34862 AA391033 AA281183 W147526 W02915 R34165 R35396 T97386 R79640 W25256 R39440 AW138025 BE178196 R26447
C03146 C03663
50 457952 44256_1 U25750 A792472 AA487379 AI872282 AA487262 R22383 AI865790 R21832 A5693628 AW571868 AA371791 R71814 T27183
458996 83645_1 BE220675 AA345821 AA009992

WO 02/098358

PCT/US02/17594

TABLE 2C

Play: Unique number corresponding to an Eos probe set

Ref: Sequence source. The 7 digit numbers in this column are Genbank Identifier (GI) numbers. "Dunham I. et al." refers to the publication entitled "The DNA sequence of human chromosome 22." Dunham I. et al. (1999) *Nature* 402:489-495.

Strand: Indicates DNA strand from which exons were predicted.

NL_position: Indicates nucleotide positions of predicted exons.

Play	Ref	Strand	NL_position
5	400481 8439853	Plus	112453-112541
	400501 9796227	Minus	12479-12619
	400713 8110874	Minus	43185-43394
10	400769 8131028	Plus	28571-29795
	400818 8698994	Plus	172844-172765,173065-173200
	400891 2842777	Minus	91448-91603,92123-92265
15	400882 2842777	Minus	110431-110700
	400965 7770576	Minus	173043-173564
	400986 8065497	Minus	63149-63319
20	400995 8098094	Plus	141186-141601
	401093 8616137	Minus	22335-23166
	401178 9438616	Minus	133663-133812
25	401192 9719502	Minus	68659-70101
	401209 7712287	Plus	164932-165112
	401405 7768126	Minus	63278-69462,69648-69958
30	401416 7452889	Minus	121456-121626
	401419 7452889	Minus	136389-135508
	401444 8346725	Plus	90895-40694,93070-93213
35	401512 7522248	Plus	153539-156557
	401563 8247910	Plus	91365-91763
	401600 4388746	Minus	27363-27518,28727-28891,29526-29731
40	401750 9828651	Plus	82143-82270,86284-85073,90596-90770,95822-96001,96688-96775,96870-96992,98046-98138
	401757 7239530	Plus	88644-89751
	401839 7656537	Plus	1015-1086,2751-2967,3241-3348,20677-26831
45	401849 7770425	Plus	129375-129483,129697-129720
	401862 3319121	Minus	53770-53979
	401868 3128781	Plus	25397-25918
50	402082 8117478	Minus	190046-190183
	402101 8117697	Plus	134308-134487,135402-135587,136421-136548
	402108 8131852	Plus	3717-3848
55	402163 8668936	Plus	166996-167119
	402185 8576022	Plus	25486-25638
	402240 7890131	Plus	104302-104527,105136-105372
60	402249 7704953	Minus	107636-107813,108694-108824,110435-110502,113182-113386
	402347 8099287	Minus	13714-15440
	402398 1905896	Plus	4476-4648
65	402469 9797107	Minus	71265-72351
	402532 9803951	Minus	180240-180558
	402559 9884273	Plus	33639-33715
70	402575 9884830	Minus	109742-109883
	402602 7238066	Plus	6785-6872,7478-7575
	402758 9213869	Plus	87638-87804
75	402786 9715046	Plus	47624-47795
	402807 6456148	Minus	101542-101660,103476-103656
	402810 6010110	Plus	12715-12866,13527-13643
80	402864 9881899	Minus	46524-46784
	403046 3540153	Minus	55707-55859,56399-60511
	403065 8748904	Minus	108532-110225
85	403217 7630969	Plus	54039-54163,55427-55623
	403218 7630969	Plus	58539-59149
	403291 7230870	Plus	96177-96436
90	403328 8469096	Minus	120478-120703
	403654 8736093	Minus	28634-28758
	403704 4962546	Minus	8860-8986
95	403708 6705981	Minus	124304-134812
	403725 7534031	Plus	86737-86843
	403739 7630882	Plus	44563-44766,48209-48403,52295-52465
100	403740 7630882	Plus	86604-87227
	403745 7630836	Plus	67819-68602
	403746 7630836	Plus	93612-93887
105	403885 7710403	Minus	53299-53524
	403893 7710581	Minus	5436-7846
	403947 7711923	Plus	38657-38817
110	404039 8698763	Plus	81889-82011
	404054 3548785	Plus	66713-69175
	404058 3548785	Plus	99397-101808
115	404108 8247074	Minus	63603-64942
	404211 5026246	Plus	185728-185885,194575-194686
	404277 1834458	Minus	91665-91948
120	404384 8887028	Minus	38055-38156,42175-42381,43436-43553
	404407 7329316	Minus	48164-48499
	404489 8113772	Plus	98183-98480
125	404627 8152087	Plus	127737-127796,128080-128210,129888-130054,132545-132969

WO 02/098358

PCT/US02/17594

	404528	8152087	Plus	135325-135486
	404661	9797373	Plus	33374-33875,33789-34008
	404663	9797133	Plus	29885-30514
5	404966	7387343	Plus	55883-56203
	405011	6139150	Plus	117359-117612
	405044	7596797	Minus	58563-60141
	405102	8076881	Minus	120922-121026
	405109	8596886	Minus	30301-30518
10	405188	6649489	Plus	134573-134678
	405231	7249032	Minus	109793-109969
	405365	2715192	Minus	119867-120372,120481-120824,121029-121357
	405387	5587915	Minus	3769-5833,5708-6805
	405396	6624129	Minus	89665-90273
15	405429	7321905	Minus	51577-51723
	405435	7408068	Minus	51704-51841,53581-53767
	405446	7687529	Plus	59138-60315
	405503	9211311	Minus	51198-51314
	405525	9558552	Minus	19699-19828
20	405579	9581957	Minus	39544-39713
	405610	5757553	Minus	71907-72000
	405802	5926004	Minus	27743-28264
	405811	6902753	Plus	5128-5248
	406180	7283201	Minus	38503-39167
25	406207	5923550	Minus	162607-162800
	406302	8575595	Plus	165961-169150,169610-169769

PCT/US02/17594

Key: Unique Eos probe/seq identifier number
ExAcc#: Exemplar Accession number, Genbank accession number
UnigenID: Unigene number
Unigene Title: Unigene gene title
Seq ID No: Seq ID number correlation for those sequences in Table 4

	Play	EnzAcz	UnigeneID	Unigene Title	Seq ID No
10	415539	EA13381	Hs.72472	BMI-1B	Seq ID No 1 & 2
	448988	UY0763	Hs.22785	gamma-aminobutyric acid (GABA) A receptor subunit 10 (GABA _A R10) human cDNA	Seq ID No 3
	406933	EA563372	Hs.46677	phosphatidylethanolamine 3-phosphate UDF-glucuronidyl transferase	Seq ID No 11 & 12
	408660	AA52575		ESTs, homologous to PCAD59 from rat	Seq ID No 13 & 14
15	405051	AA080912		gln:amd3431, Strikingly similar to PCAD59 from rat	Seq ID No 15 & 16
	404303	EA43303		gln:amd412.1, Strikingly similar to PCAD59 from rat	Seq ID No 17
	415787	HI0163	Hs.93534	ESTs	Seq ID No 18
	415599	AA17279	Hs.29429	ESTs	Seq ID No 19-21
	405770	AA57730	Hs.18515	ESTs, highly similar to PCAD59 from rat	Seq ID No 22
	420757	X78552	Hs.29915	endogenous receptor (glycylphosphatidylserine r	Seq ID No 23 & 24
	429163	AA884766		gln:amd6r10.1 Soares, NGLT1_GDC31_Homo s	Seq ID No 25
	425441	AA224172	Hs.20496	lipoprotein B (lipoprotein family member)	Seq ID No 26 & 27
	425441	Y13367	Hs.19583	phosphatidylethanolamine 3-kinase, class 2, alpha	Seq ID No 28 & 29
	432342	AA541323	Hs.115831	ESTs	Seq ID No 31
	432435	BE218606	Hs.282070	ESTs	Seq ID No 32 & 33
	432527	AW919028	Hs.102754	ESTs	Seq ID No 34
	435076	AA1812586		gln:amd25.5, gln:amd25.5 coupled receptor 48	Seq ID No 35 & 36
	438233	WS2448	Hs.58147	ESTs	Seq ID No 37-40
	439569	AA1662166	Hs.222389	CEBP1 protein	Seq ID No 41 & 42
30	440819	AB000444	Hs.202128	ESTs	Seq ID No 43
	442832	AA020500	Hs.29356	ESTs	Seq ID No 44
	447412	AI199268	Hs.19322	Homo sapiens, Similar to RIKEN cDNA D10A	Seq ID No 45 & 46
	447499	AA026580	Hs.147674	proteobactin beta 16	Seq ID No 47 & 48
	451411	AA74432	Hs.130555	ESTs	Seq ID No 49
35	451270	AA050885	Hs.206853	ESTs	Seq ID No 50 & 51

WO 02/098358

PCT/US02/17594

Table 3B shows the accession numbers for those Play's lacking UnigeneIDs for table 3A. For each probed is listed gene cluster number from which oligonucleotides were designed. Gene clusters were compiled using sequences derived from Genbank ESTs and mRNAs. These sequences were clustered based on sequence similarity using ClustalW and Alignment Tools (DoubleTwist, Oakland California). Genbank accession numbers for sequences comprising each cluster are listed in the "Accession" column.

5	Play	CAT Number	Accession
	408660	107294_1	AAG25775 AAC52340 AJ538578 AW975281 AA504886
	408651	109699_1	AAC30512 AAC75318 AA063403 AA076584 AA078952 AAC84526 AAC81861 AA113913 AA113862 AAC83821 AA134801 AA082953 AA070343
			AA052835 AAC75419 AA063293 AA071252 AA078900 AAC62836 AW974305
10	409123	110143_1	AA063403 AAC70823 AA070050
	429163	300543_1	AA884766 AW974271 AA692975 AA447312

WO 02/098358

PCT/US02/17594

Table 3C shows genomic positioning for those Pkay's lacking Unigene IDs and accession numbers in table 3A. For each predicted exon is listed genomic sequence source used for prediction. Nucleotide locations of each predicted exon are also listed.

5	Pkay 403740	Ref 7630862	Strand Plus	ML_position 86504-87227
---	----------------	----------------	----------------	----------------------------

WO 02/098358

PCT/US02/17594

Table 4:

Seq ID NO: 1 DNA sequence
Nucleic Acid Accession #: NM_001203
Coding sequence: 274..1782

	1	11	21	31	41	51	
10	CGACGAGCGT	GAGCGCGGCG	GCGCGCGCGG	GAGCGCGCGG	AGTGGGAGGA	CGCGCGCGCT	60
	GAGCGAGCGT	GAGCGCGGCG	GCGCGCGCGG	GCGCGCGCGG	GAGCTCTGAT	TTCTTATGAT	120
	CGCGCGAGCG	AGGATGAGCTA	TTTCACTGCT	TGTTCAATAA	GGTTCGAGCT	TCTGCTGATT	180
	CATACCACTT	TGCGCTCTGAG	CTATGACAGG	AGAGGAACTA	AAAMGTTAAA	CTTACAGGCC	240
	TGCGATAAGT	GAGAGACGAA	CTTCTCTGAT	ACAATCGTCT	TGGGAGATCC	AGGAAATTTA	300
	ACATCGGCGA	CGAGGAAGAA	GGAATGTGAG	AGTACAGGCC	CGACCCCGCG	TCCAGAGGTC	360
15	TTGCTTTGTA	AATGCGCTCA	CAATTCTGCA	GAGAGCTGCA	TGAGCAATAT	TTGCGGCGCA	420
	GAGCGATATT	GTTCACGAT	GATAGAGAG	GATGACTCTG	GGTTGCGCTT	GGTCACTCTC	480
	GGTTGCGCTAG	GACTAGAGGG	CTGAGATTTT	CACTCTCGGG	ACACTCCCAT	TGCTCATCAA	540
	AGAAAGTCAA	TTGATCTCTG	CGACGAGAGG	AGCAATATGA	ATAAGAGCTT	ACACCCCTAC	600
	CTGCTCTCAC	TGAAACAGAG	AGATTTTGTT	GATGCGCTTA	TACACGCG	GGCTTTACTT	660
20	ACATCTGTGCA	CTGTCTGZAG	TTTGCTCTTG	GTCCTTATCA	TATATTTTTG	TTACTCTCGG	720
	TATAAAGACG	AGCAAGACCG	ACCTGATAC	AGCATTTGGT	TAGAAGCGGA	TGAACCTTAC	780
	ATCTCTCTCTG	GAGATTCCTT	CGACGACTTA	ATTAGACAGT	CTGAGAGCTC	AGGAATGTGA	840
	TCAGCGCTCC	CTCTCTCTGT	CGAAGGACT	ATAGCTAAGC	AGATTCAGT	GGTAAACAG	900
	ATTGGAAAGG	GTGCTATGAG	GGAATTTGCG	ATGCGGAAAT	GGGTTGGCGA	GAAGTACTCT	960
25	GTGAAGATGT	TCTTCCACAC	AGAGGAGGCC	AGCTGGTTCA	GAGAGACAGA	AATATATCAG	1020
	ACAGTGTGGA	TGAGGACATGA	AAACRTTTTG	GGTTTCATTO	CTCAGATAT	CAAGGGACCA	1080
	GCGTCTCGGA	CGCACTTTTA	CTATATCACA	GACTATCATG	AAAGTGTTTC	CTTTTATGAT	1140
	TACTTAAAGT	CGCCACTCTT	AGACCTTAA	TCATATCTGA	ATTATGCTTA	CTCTTTCTAT	1200
	AGTGGCTTAT	GTCACTTTGA	CACAGAAATC	TTTATGACTC	AAGGCAACCC	AGCAATTGCC	1260
30	CATGAGACTT	TGAAAATGGA	AAACRTTCTG	GTGAGGAAA	ATGAGACTTG	CTGTATTCTT	1320
	GAGCTTGCGC	TGCGCTGTAA	ATTATTAGT	GATACAAATG	AAATGACAT	ACGACATCAAC	1380
	ATCGAGATGT	GCGCAAGAG	CTATATGCTT	GTCAGAGTGT	TGCGAGAGC	CTTGACAGCA	1440
	AAATCACTTCC	AGTCTTACAT	CATGCGTAG	ATGTATAGTT	TTGGGCTCAT	CCTTTGGGAG	1500
35	GTGCTAGGAA	GATGTGTATC	AGGAGGTATA	GTOGAGAAAT	ACGAGTCTCC	TTATCATGAC	1560
	CTAGTGCCCA	GTACGCGCTT	TTATGAGGAC	GAGAGGAGGA	TGTGTGCAAT	CAAGAGATTA	1620
	CGCCCTCTCA	CTGCTGAGCT	GATATGCTTA	TAGCGAGTCT	GGGAAAGTCT	CGGAAAGTCT	1680
	CTGACAGAA	GTCTGGCTCA	CAATCTTGCA	TCAGGCTGGA	CGGCGCTGCG	GGTAAAGAAA	1740
	ACACTTGGCA	AAATGTCAGA	GTCCGAGGAC	ATTAAACTCT	GATAGGAGAG	GAAGAATGAG	1800
40	CACTCTCTGCA	GAAAGCCACAC	AGGTACCTCT	CTGTTGTGCG	CGAGAGCAAA	AGAACTACAA	1860
	TAGATCTTCA	CGATGACAGC	CTGGAACATC	GTCTCTCTCT	CGGATGGGTT	CGAGCTCTAC	1920
	CTTTCAAGGA	CGGACCTGAG	CAAGACAGCA	GAGCTCTGCA	GAGAGGAGAT	TGTTCTGCTG	1980
	TCGTTTGTGA	GGCGGAGAAA	CGTTGGGTA	ACTTGTTCGA	GATATGATGC	AT	

Seq ID NO: 2 Protein sequence
Protein Accession #: NP_001194

	1	11	21	31	41	51	
50	MLLSAGKLN	VQTKKEGDES	TAPTPTSKVL	RCKCHHHCFE	DSVNICSTD	GFCTWIBSD	60
	DGLPLVVTSG	CLGLSGDSGF	CRDTPIPHGR	RSEICETERN	RCHDLPHPL	PLPKRHFDFD	120
	GPIHERALLI	SVTVCSLLLV	LILPCTFYFR	KRGSTRPRYS	IGLSQDETVI	PQESLRDLI	180
	EQPSGSSGSG	GELFLVQRTI	ARQIMVQKI	GEXRYGEVM	GKWRGSEKAV	KVFFTERAS	240
	WPRETRIVQT	VLNRHNLIO	FLAADIKGTG	SVPLGLITDT	YIENSLYVIL	LKSTLDKAS	300
	MLKLAYSSEVS	GLCHLTETIF	STQKGAFLAN	RDLKSNILVL	KIMTCCCIAD	LGLVXKPSD	360
55	THVEDIPFNT	RVOTERYNPP	EVLDESILNIN	HPQSTIMADM	YSFGLILNEV	ARRCVSGGVV	420
	SEYQLPHVHL	VPSDDSYEDM	REIVCIKKLR	PSFPHRNSSD	ECLAGMGKLN	TECHAINPAS	480
	RLTALRYVKKT	LAKNSGSDQI	KL				

Seq ID NO: 3 DNA sequence
Nucleic Acid Accession #: NM_004961.2
Coding sequence: 55..1575

	1	11	21	31	41	51	
65	CGCAGAGCGT	GAGCGCGGCG	CTCGCGCGAG	GTGGTCTGCG	CGGCTCTCGC	GGAAATGTG	60
	TCGACAGCTT	CTGCGCTCTG	CTGACGCTCT	CTGTTGATCG	TGCTATGAGG	GGTGAAGGGA	120
	CTTCAGAGCT	AAATCAAGGA	TGAAGCTCTT	TCCGCTGATG	TTGCTATAGG	CGCCGAGGCC	180
	CAGGCTCTTG	AAATCAAGCT	CTCTCTTGAG	GAACAAAGAT	CACTAGAGAC	TGAGCTCGGG	240
	ACGAGAGTTG	GGAATCTGCG	AGAAAGCTCT	CGATCTCTGA	ACATCATCTC	GATATATTAT	300
70	GACACCAAC	TGCGCTCTG	CTTTGAGAG	AGCCGCTGTG	TGGTCACTGT	TGAAGTCCAC	360
	CTGACAGGCT	TGCTCTCTCT	CTCTATCTTA	GACATGGAAT	ACATCTCTCA	CAATCATCTC	420
	TCCGACAGCT	GATACAGCGA	AGGCTCTCTT	TACAAAGACA	CGTTTGAGTC	TCTTGTCTCTG	480
	AATGCGAATG	TGTTGACCGA	CGTATGAGAT	CGGACACACT	TTTTTAGAAA	TCTTAAGAGS	540
	ACCTCAGAGC	ATAGATATAC	CGTCTCTCAC	CGATATGCTG	CGATCTACAA	GGATGCGAGG	600
	GGTGTGTACA	CAATATAGAT	GACCTCTGAT	CGGCTCTGAT	CGCTCATCAT	CTGACGATTG	660
75	CGAATGAGAT	CTCATCTCTG	CGCTCTCATC	TTTCTTAGCT	TTTCTATCTC	TGAGATGAGG	720
	ATGATCTACA	AGTGGGAAA	TTTCAGGCTT	GAATCATGAT	AGAGAGACTC	CTGAGAGCTC	780
	TTTCAGTTTG	ATTATTACAG	AGTGGAGAC	AAACTGTAAA	TAACTACAC	CCAGGTGTGT	840
	GACTCTGAGG	TGTAAGAGAT	TTTCTCTGAT	GTGACGAGC	GGTTTGCTCA	TGTGCTCTT	900
80	CAAACTATG	TGCTCTCTCT	CGTACGACCG	ATGCTCTCTC	GGGTTTCTCT	TTGGATCTAG	960
	ACAGAGTCTG	CTCGAGCGCG	GACCTCTCTA	GGATCATCTC	CTGTCTGAC	GATGACCAAG	1020
	TGCGGAGCTC	TTTCTCTGTA	GAATTTCCCG	CGTGTCTCTC	ATATACAGAC	CTTGATTTTC	1080
	TATATGCCCA	TCTGCTCTGT	CTTCTGCTCT	TGCGCTCTGT	TGGAGTTTGC	TGTGCTCTAC	1140

PCT/US02/17594

Seq ID NO: 4 Protein sequence
Protein Accession #: NP_004952.1

Seq ID NO: 5 DNA sequence
Nucleic Acid Accession #: NM_021984.1
Coding sequence: 572..1753

184

WO 02/098358

PCT/US02/17594

5 TGAGGGGAGT ACCTGGCGAG AGGCGCGGCT CTGCATCCAT GTCTACGCC TGGATAACTA 1680
 CTGAGAGT GTTCTGAGT TGAACCTTCT CTCTCTCAT GTCTCTTACT GGCCTGTGTT 1740
 CCTTAAGTCT TAGGTACCGC CTGCTACCTT GTGCGCGCAC CTCTCAAGTT CCGGACGAGG 1800
 TCCAGAGCCC TTGCGAAGGG AGTTCGGGGA AAGCAGCAGC AGCGCAGGA GCGACTAGAG 1860
 TTTTCTCTGC CCGATCTCCC AAACAGAGAG CTTCAGAGAG TTCTCTTTTG CTGCTCTCTG 1920
 CCGCTACTCT GCGCATTCAC TGAATTTTCT CAGCGCGCAC TTCTCAATTA TTAAATAATG 1980
 GCGCACTCTC CTCTCTTCA AGGAGCATCC GTGATGCTCA GGTGTGAAAA CACAGCCAC 2040
 TTATGTATCA GCTCTCTAAA ACCATGCTTA AGTACAGGCG GATTAGCTAT CTTCACAA 2100
 TACCTCAQAC CAGACAACTA CTGATTTTT CAGAGAGCCC ACATATGCTT TTGTAGTCTT 2160
 TTGCGCGGAG TTGTGATGAG AGCTCTCAAG TCGACGACAT AGTCTCTTCC CTATACGCT 2220
 CAGCATTAATA AGAGCTGCGG CAGCAGATA ACAGAGAGGA AGATGCTCTT TCTTTGCT 2280
 AGATTATTAT GTTCTCAGTT CTCTCTCCCT GCTACCCCTT TCTCTCGMGA TAGATAGACA 2340
 CTGCGATTAT CCGTTTAAAG AGAGGGGGGG GCGAGCAGAG ACGCTATTTG GCGACGATT 2400
 CTCTCTCTCT TCTGCTGTGT ACATCTCCCT CTCTCTTGTC GTCTCACTTT TGGCTGTGAC 2460
 TACCATCTCA ATGCTGAGT TCCATCTCA ATCTATGCT GTGTGTGATT ATAGAGATA 2520
 CTCCCTGCTT TATACGCCAC CTTCTCTCTT CTCTTTGACC CCGTGTGACT TTCTGTGAC 2580
 TTTCCCAATG ACTTCCCGCTA GCGCTGACCC AGGCATGAG CCGTGTGTGAC TCTCTGGGG 2640
 CAGAAACTCA AGGAAACTCG GTCTTGCGAC AGGCATTAAT GCGATTGAT TGGTGGCCAC 2700
 CAGCGGCACT CTGCGAGAT CTATGCACTT GCTTGACCCC TGGACCAATA AACGATCCA 2760
 CTGTATACCC GCGGCGACTC TAAACATCAC AATCAATCAA TCAAAATCCC TAAATTGTG 2820
 ATGGCATCTG AACCTTGCGA AAGCACTTTT GACAAGTTGT GTCTGATGG AGCTCATGA 2880
 TAGCTCTGTG ACACTCTTAG GCGAGGATTC TTATCCCATT TTTCGAGATG AAAACCTGAC 2940
 GTCCAGAGAT TCTGTGGGAC TGTGATCTCT ACTGGGAACT ATCCAGAGGC CACTCTGAC 3000
 CTCTCAGAGT ACCTGTAAGG GCTGAGCAGC TCGATCTCAC AAGATATCTT TCTCTCACT 3060
 CTGCTGCGAC ACCAGTGGCA AGGCCAGAA TGGCGACTTC TCTTTAGCTC AATTCTCGG 3120
 CTGAGGTGTC TCGAGCTGCC CCGAGATACA AATCTCTCT GCGCTGTAGT ACCAGTGG 3180
 ATGAAATTGG ACAAGGCCCA ATGCTCTCAT ATGCTAAGTG AAATCTGTAT CTGTAATTG 3240
 TTGGGGAGTG GATAGACTGG GGTCTCTCAT TACTTTTTG CAGCTCATG TGAJATGGG 3300
 AATATGTAA ATAAATATAT CAGCAAGC

Seq ID NO: 6 Protein sequence
Protein Accession #: NP_066819.1

35 1 11 21 31 41 51
 MYETIDIPPS QYDWERLICY NTFPESILVIA GRVVSQENIP DTFPNSKRT HEBEITWPNQ 60
 MVLVIKDGKV LYTRIMTIDA GCSLHMLFF MDSHCPLSF SSFSPENEM IYKHNFKLS 120
 IREKNSKWLK QLDFTGVSNK TEIITTFPVD FWNHITFMY SRFGYVAFQ NYVPSVTTM 180
 LSWVSPWIKT ESAPARTSLG ITSVMITLT GTPSRGNHPR VSYITADLYF IAICTFVCTC 240
 40 ALERFVPLSF LIYNQTKASA STGKREHRII BSAARHTRAR SKACBAGHGF AFQVQIVTTE 300
 GQDSBBSPLF SAQPTPVSG PPSPLSICX LACBHCXFC KXTQNHVDC BSGTQKRL 360
 CHVYRLNLY SRVCFPVTF FFWLYLVLC LNL

Seq ID NO: 7 DNA sequence
Nucleic Acid Accession #: NM_021987.1
Coding sequence: 572..1657

50 1 11 21 31 41 51
 GCGAGAGGAT GAGCGCGGAC CTCCGCGCAG GTGCTCGGCG CGGTCTCGCC GGAATGTGTT 60
 TCCAAAGTTC TTCAAGTCTT CCTAGGCATC TTATGTATCC TCCATCGAG AACATGTATA 120
 CAGAGAGATG CTCGAATCAT AAGGTGACAG CTGATGAGTT GTCAAAAAAT GACCAACAGC 180
 TGTAAAGAAA AGCAAAATCA AGGACCGDAA TGTAGAGAGG ACTCGTAAG CCCCTTTGTT 240
 55 CACTGCTCTC CAGCAAGAGC AGCATATACC GAGCTCTTA CAGCATCGAG TCGAGGAGCC 300
 TCGAGCTGAA TCAAGGAATG AAGCTCTCTC CGGTGATGTT GTCTATGCC CCGAGCCCCA 360
 GCGCTCGGAA AATCAAGCTC TCTCTGAGCA AACAAAGTCA ACTGAGACTG AGACTGGAG 420
 CAGAGTTGAG AAACGCGGAG AAGCTCTCTG CATCTGACAC ACTATCTGTA GTATTATAGA 480
 CCAACAAGTC CGGCTCGGCA TTGAGAGAGA TCTCACTCTG GTCTACTGTT AGATCTCCCT 540
 60 CACAGCGCTT GGTCTCTCT CTATCTCTAGA CATGGAATAC ACGATTGACA TCACTCTCTC 600
 CCGAGCGCTG AATTCTAAGA GGAACCCACA GATGAGATAC ACGATGCCCA ACCAGATGTT 660
 CCGCATCTAC AAGTCAAGCA AGGWTGTGTA CAGATATAG ATGACGTTG ATGCGGATG 720
 CTCACTCCAC ATGCTCGATAT TTCTCAAGGA TTCTCACTCT TACTCTCTAT CTCTCTCTAG 780
 65 CTTTCTCAT CTCTGAGATG AGATCATCTA CAGAGTGGAA AATTCAAGC TTGAATGAA 840
 TGGAGAGAAC TCTCGAGAGC TCTTCAGTT TGAATTTACA GGAATGAGCA ACMAAATGAG 900
 AATATACCA ACCCGAGTGT GTGACTCAT GTGATGAGAC ATTTCCTCA ATGTGAGGAC 960
 GCGATTTGTC TATCTCTCCC TTCTCAAGCT TGTCTCTCTG TCGATGACA CGATGCTCTC 1020
 70 CTGAGCTCTT TTTGTATCA AGACAGATCT TCGTCTCAGC CGAGACTCTC TAGGGATCAC 1080
 CTCTGTCTTG ACCATGACCA GGTGCGACAC CTTTCTCTCT AAGAAATTC CCGTGTCTC 1140
 CTATATCA CA GCTCTGATAT TCTATATGCG CATCTGACTC GATCTCTGCT TCGGCTGCT 1200
 TGTGAGATTG GCTGTGCTCA ACTCTCTGAT CTGACAGCAG ACGAAAGACC AGCTCTCTC 1260
 TAACTCTGTC CATCTCTGTA TCAATAGCTG TCGCAAGGAC TCGATCTGCT GAGCTCTCTG 1320
 AGGCTGTGCC GCGCAACATC AGGAAGCTTT TGTGTGCCAG ATATGTACA CCGAGGGAAG 1380
 TATGATGAGG AGGCGGCGCTT CTTGCTCAG CCGAGCGGCC CCGAGCGGAG GTAGCCTGGA 1440
 75 GGTCTCGGCC AGCTCTCAT CTAGACTGCG CTGCTGTGAG TGTGTCAGC GTTTTATGAA 1500
 GTACTCTCTC ATGCTCTCCC ATCTCGAGCT CAGTATGACT CAGAGGCTCT GCTCTCTCT 1560
 CCGATGCTAC GCGCTGAGTA ACTACTCGAG AGTTGTCTTC CCGATGACTT TCTCTCTCT 1620
 CAATGTGCTC TACTGCTGTT TCTGCTTAA CTTGTAGTA ACGACTGTA CCGCTGTGG 1680
 CAGCTCTCTC AGTTCGCGAG GAGGTGCGAG CCGCTTGACA AGGAGTGA GGAAGAGCAG 1740
 CAGACGAGAC AGAGCGATCT AGATTTTCTC CTGCGGCTCT CCGGPAAGG AAGCTGCGAG 1800
 80 AGGTTTGTCT TTGCTGCGCC CTCTGCGCTA CCGTGGCCAT TCGATGAGTT TCTGAGCAG 1860
 ACAATTTCAC ATATATTAATA AATGGGCCAC CTGCGCTCTC TTGAGGAGC ATCGGATG 1920
 CCGAGTGTTC AAAACCGACG CCACTGATG ATCAGCTGCC TAAAGCATG CTAATAGTCA 1980
 GCGGATTAG GCTCTTCCA ACATGTCTGA CCGACAGACA ATTAATGCTT TTTTCGAGA 2040

WU 02/098358

PCT/US02/17594

5
10
15
20

```

GCCACATTT  GCGTTTGCG  TGCCTTGCG  CCGATCTCG  CCGACCTTC  AAAGTGACC  2100
GACTATGTC  TTCTGCTCT  CTGACACCT  ATGAGATCT  TGACACGAG  TGAATACAG  2150
GGAAGGATC  CCTCTCCTT  GTCGAGATTA  TTAATTTCT  AGTTCTCTCT  CCGCTGACC  2200
CCTTCTCTCT  CAGATAGATA  GACATCGGA  TTATCCTTT  AGAGAGAGG  GGGGGACGA  2250
AGAGAGCCTA  TTGGGAGAG  CATTCTCTC  TCTCTAGTG  TGACACATC  CCGCTCTCT  2300
GCTGGCCCA  TCTCTGCTC  GCGATGCGA  TGCARGCC  TGCACCAAT  GGTATCTAT  2400
TTTCTGGGT  GATGAGATA  ACTACCTCT  CTTTATATG  CCACCCCTT  CCGCTCTCT  2450
GACCCTGTG  ACTCTTCTG  TAACTTCCC  AGTAGCTTC  CCGAGCCTG  ACCAGGCACT  2500
AGGCTCTGT  GACTCTCTG  GCGCAGAAA  CTAAGGAAC  TCGCTCTTC  AACAGGCACT  2550
ACTGGCATT  GATGTGCGT  GACACGGGC  ACCTCTCTA  GATTCTATCA  CTTCTGATG  2600
CCTCTGAT  ATGACCGAT  CCGCTCTAT  ACTGAGCA  CTTCTAGAT  CAGATCAAT  2700
CAATCAATT  CCTCTAAAT  TGTATGGAC  TGGAACTTG  GCAAGCACT  TTGACAAAT  2750
TGTCTGAT  TGGAGCTCA  TGTATGCTT  GTACATCTT  TAGCGAGA  TCTCTATCC  2800
CAUTTTCAG  ATGAAAGCC  TGAATCAG  ATTCTCTG  GACTCTGAT  CTGACTGAA  2850
GCTATCGAG  AGGCACTCT  CACTCTGAG  ACCACATAT  AGGCTGAG  CAGATCAAT  2900
ACCATATTC  TCTCTGTGA  CCTCTGCTG  CACACAGTG  GCGAGGCCA  GATGGGAGC  3000
CTCTCTTAG  CTCATTTCT  GGGCTGAG  TGCTGAGCT  GCGCCCAAG  CCAATCTCT  3050
CTGGGCTGA  GTACCCAG  GGAATGAAT  TGACATGCG  CGAATGCTT  TATATCTAA  3100
TGAAATCTG  TCTCTGATC  TTGTGGG  GTGAGTAG  TGCGCTCC  ATCTACTTT  3150
TGTCAATC  ATCTGAAAT  GGAATAATG  TAAATAATA  TATCAAGAA  GC

```

Seq ID NO: 8 Protein sequence
Protein Accession #: NP_058822.1

25
30
35

```

1 11 21 31 41 51
MEYTDIIPS  QWSEKSH  HEIYEMQW  RIYKDKWLY  TIRMTDAGC  SJMLAFPMQ  60
SISCLPFS  FVFEHRY  FHEFELEIN  ACTGKAGLT  DPTWEMITE  TITITPQW  120
VMTFFRVSR  FEGGVAFWY  VFSSVITML  WSEWIKIE  AFARTSLOIT  SVLZMTLGT  180
FERKHFVRS  YITALDPIA  ICFVPTCAL  LEFAVNFEL  YMTQAHASP  KLEHPRINSR  240
AARTRARS  ACARGGEP  VOQIVTEGS  DGBRFSCBA  QPPSPGSGS  GPELSCSLA  300
CCEWKAPEK  TFCWVDCBG  STWQGGELCI  HYELDNIGR  VVFFVTFFFF  NVLWLVCLM  360
L

```

Seq ID NO: 9 DNA sequence
Nucleic Acid Accession #: M0_021990.1
Coding sequence: 1509..2490

40
45
50
55
60
65
70
75
80

```

1 11 21 31 41 51
GCCAGAGGT  GAGCCCGAC  CTCGCCGAG  GTGCTCGCG  CGGTCTCGC  GAAATGTTG  60
TCCAAAGTC  TCTCAGTCT  CCTAGGCAT  TTAATGATC  TCGAGTCAG  AACATGTAT  120
CAGAGAAAT  CTCGAATCA  AAGGTATAG  CTGACGAT  GTCAAAAAT  GACCAAGCG  180
GTATAAAGA  AGCCAAATCA  AGAGCTCGA  TGTAGCAG  AGCTCAGA  CCGCTCTGT  240
CACTCCCTC  CAGCAGAGC  AGCACTAT  GACATCTA  CAGCAGAT  GGTPTTATA  300
CCTCGCAGA  TGCCCTTAA  CATTTTTGT  TAACTCAAT  ATTCTACTA  ATCTCTCT  360
TTTTCTGCG  TGTGTGCA  GCGTCTGAG  CTCAGGTGG  ACTCTGTT  GCGAGCCAGT  420
TCTCTGATG  CTCTCTGCG  GTGAGGACT  CTTGCTTTC  CTGTTAGAC  ACCCAAGAG  480
GCTCTCTT  AGCTCTCT  CTTTCTCT  CTCTCTCT  CCGCAGTCA  ACGATPTTA  540
CACACCAAC  AAGACGCCA  AATATTCOA  CAATTTCTG  GTCTCTCT  GAGAGGCCG  600
CTCTGCTTT  TCCCTCTAG  CCGGCCCTC  TCGCTCTCT  TCACTCTG  TTGTGTCTG  660
GAGCTGAG  TAGAGGCCA  GCGACCCAT  ACTAGCAAA  CGCGCCAG  GCTCAGAGCT  720
AATGGCCCT  TCTCTCTAG  GGTGACAT  CTCTAAAT  CAGGTCTTG  GTTTTGTGA  780
TTTCTATA  AATAAAGAT  TATCTATA  AAGAGGAGC  CATZAGAGT  CCGAAGAG  840
CAGCAGGT  TTAAGAAAT  TCACAGCT  AATCTCTAC  TGTCTATA  TTGCTATTA  900
CGAGTCACA  TTTACTAG  TTTGTGTT  AATATTTT  TTGTTTCT  GTTCTCCGA  960
GAGCAGTAG  TGTGGGCC  TACAGATTC  AAGCAGAG  TTAATTTT  GTTGAATGT  1020
TCTATGTC  AGGACATCA  GACTGATCA  AGAGTAGAG  CCGTCTCT  TGTGTTCT  1080
TAGTGCCCC  AGCCCGAGC  TCTGAAJAT  CAGCTCTCT  CTAGAGAAC  AAGGTCACT  1140
GAGACTGAG  TGGAGACAG  AGTTGCCAA  CTCAGAGAG  CCGTCTGAT  CCGTAACAT  1200
ATCTCGATTA  ATTATGACA  CAAATGCG  CCGTGATG  GAGAGAGCC  CACTGTGTT  1260
ACTGTGAA  TCTCTGTA  CAGCTCTG  CCGTCTCT  TCTTAGACA  GATATGACC  1320
ATGACATCA  CTCCTTCCA  GAGCTGTAT  GAGAGAGCC  TCTGTACA  GACACCTTT  1380
GAGTCTCT  TCTGATAG  CATGTGTG  AGTCAGTAT  GATCCCGGA  CAGCTTTTT  1440
AGGATTTTA  AGAGACCCA  CAGAGTAG  ATCCACAG  CGAACAGAT  GGTCCGACT  1500
TACAGAGTT  CAGAGGTGT  GAGCTGAT  AGATGATCA  CCGTCTCT  TACTCTCT  1560
CAATCTCA  GATCTCAAT  GATCTCTCT  CTCTCTCT  TACTCTCT  TACTCTCT  1620
TATCTGAGA  ATGAGTAT  CTCAGATG  GAAATTTCA  AGCTGAAAT  CAGTAGAGAG  1680
AATCTGTGA  AGCTCTTCA  GTTTGATTT  AONGAGTGA  GGAACAAAC  TGAATTAAT  1740
ACAAACCGA  TGTGATCT  GAGCTGAT  CAGATTTCT  TGAATGAG  CAGAGGTTT  1800
GCGCATGTC  CTTTCAGAA  CTAATCCCT  TCTCGCGA  CAGCAGAT  CTCTGAGTT  1860
TCTTTTGA  TCAAGACAG  GTCTGCTCA  CGCCGAGCT  CTCTAGGAT  CAGCTCTGT  1920
CTGACCACT  CAGCTTGG  CAGCTTTCT  CTAAGAAAT  TCGCGGTGT  TCTCTATAT  1980
AGAGCTCTG  ATTATGATA  CGCAGTCT  TGTCTCTCT  GCTTCTGCT  TCTGTGAG  2040
TTTGCTCT  TGAATCTCT  GAGCAGAG  CCGCTCTCT  TCTTAAGCT  TCTTAAGCT  2100
CGCATCTCT  CTCTCAATG  CCGTCCCAT  GTGCGATCC  GTGCGATCC  CGAGCTCT  2160
CGCCGCCAT  TTTTGTGCT  TTTTGTGCT  CAGATCTCT  CCACTGAGG  AAGTAGAGA  2220
GAGAGGCCCT  CGCTCTGCT  AGCCAGAG  CCGCTCTCT  CAGGTAGCC  TGAAGTCCC  2280
GAGAGGCCCT  CGCTCTGCT  GAGTCTCT  GAGTCTCT  AGGTTCTA  GAGTCTCT  2340
TCTGATCTCT  CCACTGTA  GGCAGTACC  TGCACAGAG  GCGCCCTCT  CATCTACT  2400
TAGCCGCTCT  ATAACTACT  GAGATTTGT  TTCCAGTGA  CTCTCTCT  CTCTCAATG  2460
TCTCATCTCT  GTTTTGTCT  TAACTGTG  GTACAGCTG  GTACCTGTC  GAGCAAGCT  2520
TCAATTTCCC  CAGAGGTCT  AAGCCCTTGT  CTAAGGAGT  TGGGGAGAG  GAGCAGAGC  2580

```

WO 02/098358

PCT/US02/17594

```

ACGAGGAGCG ACTAGAGTTT TTCTGCCCC ATTCGCCCAA CAGAGGCTCG CAGAGGGTTT 2640
CTGTTCCTCG CCCCTCTCCG CTACTCTGCC CTACTCTACGA GTTCTCTCG CAGACCATTT 2700
CAAATTAITA ATAAATGGCG CACCTCCCTC TTCTTCAAGG AGCATCCCTG ATGCTCAGTG 2760
TTCAARACTA CAGCACTTA GTATCAGCTC CCTTAAACCT ATGCTTAAGT ACAGCGGGAT 2820
TACATCTCTT CAGCAATATC TGACACACCG ACAATTAATG CATTTTTCRA GAAGTCCACT 2880
ATGCTCTTTC CAGCACTTTC GACCACTATC TGCGCTCAGC CTCGAAGTCC ACCCACTACT 2940
TTCTTCTATA TACTTNSCAC CTCAATAAGA TCGTGGGAC CAGTATACCA GAGAGAGAG 3000
ATCCCTCTCC TTTSGTGAGA TTATATATGT CTGAGTTCTC TCTCTCTGT ACCCTTTCT 3060
CTCCAGATAG ATAGACATCG GCATTAATCC TTATAGAGAG GGGGGGGGCA GCAGAGAGAC 3120
CTATCTTGGA CACACTTCTC GCTCTCTGCG TCGTCTGAGA TCTCTCTCTC CTCTCTACT 3180
CGATCTCTCG TCTGACTAC GAATTCGAGG CTTTCTATC AATGGSTATC CATTTTTCAG 3240
TGTGATATA CTACTACTCT CTGCTCTTAT ATGCGAGCTC CTCTCTCTC TTGACCCCTC 3300
GTGACTCTTT CTGTAACTTT CCGATGACTT TCGCTAGCCG CTGACGAGCG ACTAGGCCCT 3360
GTGACTCTCC TGCGGCGAAG AAATTAAGGA AACTCTGCTT TCGACAGCGC ATTAATCCGC 3420
ATTGATCTGT GCGTCCGAG GCGACACTGT CGAGCTTATG TCACTCTGCT GACCTCTGCA 3480
CCCAATAACC AGTCCACTGT TATACCCGGG GCACTCTAAC CATCAATAC AATCAATACA 3540
ATTCCCTTAA ATTGTATGCG CACTGGAATC TTGCGAAGC ACTTTTGACA AGTGTGTCT 3600
GATTGAGCT TCAATGATAG CTGTGACACT CTTAAGGCGA GQATCTTAT CCCCATTTG 3660
AAGAGAGAAA CCCGAGTACA CAGATTTCTG TGCGACTCTG GATCTCTGCG GAGTATATCG 3720
AAGAGAGAAA TGTCACTCTC TAGACACACT GATAGGCTTA GACGCTCAG TTCACATAGA 3780
TTCTCTCTCG TCACTCTCG TCGCACCA GCTGCGAGCG CCGAATATGC GACCTCTCTT 3840
TAOCTAATCT TTGCGGCGCT AGGTGCTGAG ACTCGCCCCA AGATCAAAAT TCTCTGCGCT 3900
GTAGTAACCC AATGGAATGA ATTTGGAGCT GCGCCGAGCT TCTATATCT TAAGTAGAAT 3960
CTGTCTCTCT AATTTTGGT GGGTGTGATG GGTCTCTTAT TTTTCTACT TTTTCTACT 4020
ATCATCTGAA ATGCGGAAAT ATGTAAATAA ATATATACG AAAC

```

Seq ID NO: 10 Protein sequence
 Protein Accession #: NP_068830.1

```

30 1 11 21 31 41 51
MYETIDIPPS QYDWERLCY KDTFESLVLN SVRQVSLNP STFFNSKRT HIEHETMPWQ 60
MVRILYKDGKV LYTRMTIDA GCSLHMLRFP MUSHSCPLSP SSFYENENM IYKWNFKLE 120
IHEKNSHKLFP QDFITGVSNK TBIITTPVED PMWHTIFFYV SRFPYVAFQ NYVPSVVTMM 180
LSWVSPWIKT ESAPARTSLG ITSWLTMITL GTPSRKGFPR VSYITADPEY IALCFVFCFC 240
ALLERAPLRF LIINQYKARA SFYRREPHEN SRBAATGHR SRACGAGHGF AFVQIVVTE 300
GQCEHFPFC SAGSPSCF PEPSPSLCK LACCEKCLFP KEYTPNFFCC BSTWQOQRL 360
CHRYLENDY SRVFPVTFF FNNVLYHLVC LNL

```

Seq ID NO: 11 DNA sequence
 Nucleic Acid Accession #: NM_001076.1
 Coding sequence: 22..1614

```

45 1 11 21 31 41 51
TTCCGCAACA GTAGACGACG GATGCTCTCG AAATGGAGCT CAGTCTTTCT GCTGATACAG 60
CTCAGCTTGT ACTTATGCTC TGGAACTGTG GAAAAGTTCG TAGTGTGCC CACAGATATC 120
AGCCATGAGA TAAATATAGA GACAATCTCG GRAGAGCTTG TTGAGAGGG TCAATGAGTT 180
ACTGCTGTGA CACTGCGGCG TCTGACCTTT GTCAATACCA GTAAATCAG TCTTATATA 240
TAGAGATGTT ATCTCAATCT TTTAACATAA AATGATTTGG AAGATCTCT TCTGAAATTT 300
CTCCATAGAT GGAATATATG TTTTCAARA AATCAATTTT GGTCAATTT TTCAATATA 360
CAAGATATGT GTTGGGAATA TTATGACTAC AGTAACAGC TCTGTAAAGA TCGATTTTGT 420
AATAGMAAC TTATGATGAA ACTACAGAGG TCAAAATTTG ATGCAATCTT GCCATATGCC 480
CTTAATCTCT TGTGAACTCT ACTGCTGABA CATTATACCA TACCTCTTCT GTATGCTCTT 540
CGATCTCTCG TCGCTATCAC ATTGAGAGG AATGATGGAG GATTCTGT TTCTCTCTCC 600
TATGTACTGT TTGTATCTCG AGAATTAAGT GATCAATAAG TTTTATGGA GAGATATAAA 660
AATATGATAC ATAGCTTTTA TTTTGACTTT TGGTTTCAAA TTATGAGTCT GAAGAGATGG 720
GACCACTTTT ATGCAAGAGT TCTAGAGAGA CCCATCACTC TATTGTGAGC AATGZGZAA 780
GCTGAATCTG GCGCATCTCG AACATATGG GATTTGAAT TTCTCGGCC ATPTCTIACA 840
AATGTTGATT TTGTGAGAG ACTTCACTGT AAACGAGCCA AACCCCTGCC TAAGCAATG 900
GACAGCTTGG TCGAGACTCT TGGAGAAATG GTATATGTGG TGTTTCTCT GGGGTGAGT 960
ATCATATACA TGTGAGAGA AATGCTCAAC ATATGTGTCG TCAAGAGCCA GCGAGTCCA 1020
CAAGAAGCTC TATGAGATTT TGTATGCGAG AAGCAAAATA CATTAGTTC CATATCACTA 1080
CTGTACAAGT GTTATCCCCA GAATGATCTT CTGTGCTATC CCMAAACCA AGCTTTTATA 1140
ACTCATGGTG GAGCAATATG CATCTAGTGG CCGATGATCC ATGAGATCCC TATGTGTGAG 1200
ATTCCCTCTG TCGCCATACA AATATATAC ATCTCTACCA TCGATGCTAT CAGATCTCCA 1260
CTCTCTTGG ACTGATGAG CAGTCTCAAT AGAGATTTTC CATATCTATC GAATGATCTC 1320
AATTAATGACC CTCTCTATAA AGAGATATCT ATGAAMTAT GAGAATATCA TATGATCCA 1380
CCMATGAGCC CCGTATGATCG AGCATCTCTC TGGATATAGT TTGTATGCG CCACAAGGA 1440
GCGAGGACC TTGATGATCG AGCTACAC CTCACTTGA TCGATGATCA CTCTTGGAT 1500
CTGATACGCG TCGCTCTGAG CGATCTGCGA ACTGATGAT TTATATGAC AATATTTGCG 1560
CTGTCTTOTT TCGCAAGCTC TGCCAAACA GGAAGAGAGA ACMAAGAGA TTAGTATAT 1620
CAAGAAGCTG AATGTGAATG ACTCAAGAT GGGACTCTCT CTTATTTCA CCAATGAGGG 1680
TTTTAATGCG AGGATTTCTT TTTCTCTGTG ACGAAATCTT TTATCAAC TTAATCTTTT 1740
AAGCAAGT TTATCTTACA GGTATTTTAT AGCTCTCTTA GTTGAGATA TTCTATCT 1800
ATGATTTTAA ACTATCTAAA AATACATATG GCGAGAGAT ACCTTTATCG GATATACCA 1860
ATGTTAATG ACGATTTACT GGATCGAGCA GCGACATGG TACATTTGTA TACATATGTA 1920
GCTACACCTT COTCTGCGAC ACTGTACCTTA AACTCTAAG TACATTTTAA AAAAGAGAA 1980
AAAAAAGAT ACTACTCTCT TTTTCTTAA CAGAGAGAA AATATGAGA TGGAGACAC 2040
TTCTACTATT GATCTGAAA ATAAAGTCTC ATCTAGCCA TAAAAAANA

```

Seq ID NO: 12 Protein sequence
 Protein Accession #: NP_001067.1

WO 02/098358

PCT/US02/17594

```

1      |      |      |      |      |      |
11     |      |      |      |      |      |
21     |      |      |      |      |      |
31     |      |      |      |      |      |
41     |      |      |      |      |      |
51     |      |      |      |      |      |
5      |      |      |      |      |      |
10     |      |      |      |      |      |
15     |      |      |      |      |      |

```

Seq ID NO: 13 DNA sequence
Nucleic Acid Accession #: NM_014109.1
Coding sequence: 651..1739

```

1      |      |      |      |      |      |
11     |      |      |      |      |      |
21     |      |      |      |      |      |
31     |      |      |      |      |      |
41     |      |      |      |      |      |
51     |      |      |      |      |      |
20     |      |      |      |      |      |
25     |      |      |      |      |      |
30     |      |      |      |      |      |
35     |      |      |      |      |      |
40     |      |      |      |      |      |
45     |      |      |      |      |      |
50     |      |      |      |      |      |

```

Seq ID NO: 14 Protein sequence
Protein Accession #: NP_054828.1

```

1      |      |      |      |      |      |
11     |      |      |      |      |      |
21     |      |      |      |      |      |
31     |      |      |      |      |      |
41     |      |      |      |      |      |
51     |      |      |      |      |      |
60     |      |      |      |      |      |
65     |      |      |      |      |      |

```

Seq ID NO: 15 DNA sequence
Nucleic Acid Accession #: AK001536

```

1      |      |      |      |      |      |
11     |      |      |      |      |      |
21     |      |      |      |      |      |
31     |      |      |      |      |      |
41     |      |      |      |      |      |
51     |      |      |      |      |      |
70     |      |      |      |      |      |
75     |      |      |      |      |      |
80     |      |      |      |      |      |

```

WO 02/098358

PCT/US02/17594

TTTGATAAATA TGAATTTGGG CCCAAATCT CTCTCAAGCT CTCTCTGGGA GTCTATTCTT 780
GTCTCAAGAG TGAAGAGCTGA GTGTGTGAGT AACCTGCTGG GTGTGTGTGG 840
CTCATGCTGG TAACTCCAGC ACTTTAGAGG GCTGAGGCTG GAGATTGCT TGAAGCTAGG 900
AGTTTGAACG CAGCTTGAGC AACATAGTAA GACCTGTGCT CTATTCTAAA AAAACAAATA 960
AGTTAAAGAG ACTGTAGAGG GGCAGAGAGG GTACAGAGGG CACACACATA CCGTGTTCAG 1020
ACAGCTGGGA TCCGAGGCTC AGGAGACCTT GAGACAGTGA AACAACTCT AATATATATC 1080
ATTTTTCAT CATTGACATA ATATTATGAT TGAACAAAGA TCAATTGAGC TCAAAACCTT 1140
AAAGTGACGT TCTCTGCTCT ATGAGAGTGT CATTCTTTTA TTCTTTTAGT TCCATAATAA 1200
ATTTCTTTTT ACTTAAAAAA ACTTATAGTT TGAATGAAGG TGAGATATAT ACCTCATCTC 1260
AAGAAATCTT CACACAACCA CTATTATATT ACAGAAAGGA AATCAGTAT TTTCAGTGGG 1320
AGACATATGG CCATCTCCAG CTATCTGAAG TGTCTGAAGC TGACTGTAC CATTATGACA 1380
CAAAACACAG TGAAGTATAT CCGTATATGA TACACTAAAA AGGCACGCTT CTCTCTGACA 1440
TTGTCGACAG AAAAATGTGG TAGCTGACCA CTGAACTTAA TAAATGAGCA ATGTCAAGCA 1500
AATACAAATC CAGGTGACCA GTCTGCAAGG TAACTATCAT GTACTCTTCA ACATATGATC 1560
GACCTAGCT ACTCAAGGAG CTGAAGTGGA ATATTGTGT GAGGTCAGCA GTTCCAGATC 1620
AGCCTGGGCA ACATCATGCG ACCCATCTCT TAAAAACATC TTTTAAAAA TGAAGCAAGT 1680
GTGGTAGCAT GGCACCGTAG TCCAGCTAC TCAAGAGCTC TCAAGAGCTC GAGGCGAGAG GATGTTTCA 1740
ACATAGAGGA TCGAGGCTGC TGTGAGCTAT GATGCTGCTA CTGACCTCCA GCGTGGAGTA 1800
CAGCAAGATC TCGTGTCTTC AAACACACAC AAGAAAGTGA AACAAACATA AACAAAGAT 1860
AAGTAAATA TGCACATCA AAGTGAAGA AAAATGAGT GACTGTGAAA ATCTTAGAAA 1920
AGTACAGCCA TACCTCAAG ATATTGTAGA TTTGATTCGA GACCAACCA ATAAAGCAGA 1980
TATGTGATCA AAGTGAATCA CACAATGTGT TTTGTTCCT TGTGAATATG AAGTATATAT 2040
GGCTGGGTGT TAGTGCTCAT GCTATATAT CAGTATCTT AGAGACGGA GGCCTGAGGG 2100
TCACTGAGC CCGAGTATGT TGTGATGAC CTGGCTCAT GAGAGATCT TGTCTCAT 2160
TAAAAAAGA AGCTATGTTT ACATACACT ATAGTCTATT TAAAGTGTGA AATGCGTGA 2220
TGTCTTAAT TTTAAAACTC TTAGTGCTGG CTGGTCTCG TGGCTCATC CTGTAACTCC 2280
ATCACTTTGG GAGGCCAGGA CAGTTTATAT ACTTGAATTC AGAGTTTCA GACCAAGCTC 2340
GACACAGCG CACACATCAT CTTTAAAJA AAGAAAGAA AAGCAAAAC AGAAGGAAA 2400
AGAGAAAAA CTACTGTCTG CCTTACTCT AGCTCAATC ATTTAAAC

Seq ID No: 16 DNA sequence
Nucleic Acid Accession #: CMT cluster

1 11 21 31 41 51
CTTTTCTTTT TTTTCTTTT TAAAGAGAC AGGTTCTCAG GGTGTGAGC AGGATGCTC 120
GAGCTCTGG AGCTATGAG CTCTCTGCT TGCTCCGCA AGTGTCTGG ATTCACAGCC 60
TGAGCAGCTG CACCAAGCCC AAGGTTTTT TTAACAGGT TCTCTCAGC AATTCTAGTA 180
TCGAGATATA GGCACATCAT AGACATCACA CAGGCTGTA CTCTATACT CTGGTGAATA 240
40 CAGAGATTTC CTGAGCTGCT TGAAGAGCTA CAGCTTTCG TCTTAAATCA GTGTTTTCAG 300
CTATGAGCT CTGCTGCTGCT GCTCTGAGT TCTCTGAGC AGAAAJAAC TTTCATTTT 360
TTTTTGCTTA CATTGACATA AATGTAAAGG CTAACTCTTA TATTAACCTG TTTATTTCTCA 420
TAAATCTTAA TGGCTGTTT TCTGGCTGTA ACCAAACCCA GAGCTATAAG AATGATAACC 480
TTCAAAATCG ATTAATTAG AGATCATATA ATGGAGCTGT TTTAATTCTA TATTTCTTCT 540
45 TTTATGATT AATAAGAAA TTTT

Seq ID No: 17 DNA sequence
Nucleic Acid Accession #: CMT cluster

1 11 21 31 41 51
GGCAGAGAA GACGCCACAT CCCCATTAT AGAAGAGCTA ATAAATTTCC ATGATCACAC 60
ACTAATATCT GTTTCCTTAA TTAGCTCTCT ATGCTCCATG ATCATCTGCG TAAATATAC 120
55 AAGAAATCTA AGCCAGAGTA GCTCAATGGA TGCCAGAGA GTTGAACCA TTTTAACTAT 180
TCCACAGCTC GTATCTCTTA TCAATATGTC TCTCCGCCCT CTACGATCTC TATATATAT 240
AAGAGAACTC AACACCCCG TATTAACCGT TAAAAACATA GAGCAACAT GATACGAA 300
CTAGAAATAT ACTGATGAG AGAGACTTAG TTGTGATTTA TATATAATCC GAAACAGGA 360
CCTAAAGCT GTGAGACAC CACATCTGGA AATGATAGC AGTATGCTC TGCATATGA 420
ACTTCCACTC COTATATTTA TTTCATCTGA AGACTGCTC CACTCAZAGG CAGTCCOCTC 480
CCTAGAGACT AAATCTGATG CCACTCCAGG CAGACTAAAT CAGCAGAT ACATCAACCG 540
60 ACCAGGGTTA TTCTATGCGC AATGTCTGAA TTGTGAGCT TACCTATGCT TTTTTCGACT 600
GTCTAGAAAT GGGTCTTAA ATATTTTCGG TACTGTGCTG

Seq ID No: 18 DNA sequence
Nucleic Acid Accession #: CMT cluster

1 11 21 31 41 51
GTGTACTCA GAGCAAAAT ACAGAGTATT TATTCAITTC TTCCCACTAG AAGGACACAC 60
70 TGTCTTGGGA CAGCAAAATG AATCATGAGT TGTCAAGAGT TGTCTTGGGA AAGATGATCA 120
TGAATCTCTT TTGAGGGTGT GCAATATGAT ACAGAGTCTC ATCACTCGGG GCGACATCA 180
GCTTCTGACG TTTCTGCTCC TTTAAACGTA ACTGAGCTTC TTCAAGTCTA ATCTGAGGA 240
TAGCAGAGGT TTTCTGCTAG TTTCTTTCAG GGCATCATTA GAATTTCCGG CGCATCCATC 300
TGAATATGCG ATGCTGTGTA TACTCCAGT GTTCAGAGAT GTAGCTTCTT GGAATTTCTG 360
75 CAGCTCTGCT TCCACATGA ATATGTTCTA CAGCTGTGTA GCAATATTA ACTGGATGTC 420
CAGTCAACAT CAGTCAAGAT TTTATTAAC TCAAGAGAGT AGCTCTATAG TATTAAGAG 480
GCTTGAAGCA AATCATGCTC TTGCAATGTC CCACTGTGTC GACAGAGAG GACAGCTT 540
CGAAATATCC GGTGAGAAAT ACTTCCAGT CAGGCTGAG GACAGCGCG GGCACAGAG 600
80 CAGCTGTCTA GCGCGAGAG CAAACCGCTC GAGCAGCTC ATGGCGCCA TGG

Seq ID No: 19 DNA sequence
Nucleic Acid Accession #: CMT cluster

WO 02/098358

PCT/US02/17594

	1	11	21	31	41	51	
	TAGTCAGCAG	AAATACCTTA	ATTTCGCTTT	TCCATAATAC	TGGTATTCCA	TAGAAGAAAA	60
5	TTTCTTTATTA	AAATATCTATA	CTACATCAATC	GGACACACAGA	TTACATAAAGT	TTGCATATGGT	120
	CCAAATTTCTG	CTTAACTTCTG	TAAGAGCAAT	TGTAATCTTA	TTTTCGCGAT	ATTCATATCTA	180
	TCTATCTATT	ATTGTGATCG	TAACGCGAAT	ACTTCTAAGG	AAAGCGATGC	ATATATATTAC	240
	TTTAGTCAAG	CATTCAAGTA	AGGCAATAT	CAAACTCTTA	TCCCAACATT	TTACACTTGT	300
	AACAGATGA	AGGATGAGGT	ACAAATATCA	TTTTTGGCAA	TTTACTATTA	AGGCGCATAA	360
10	TCTATTTAGG	GGGCTTAGG	GCCATATAT	ATATATATAT	ATTTTGGAC	A	
Seq ID NO: 2 DNA sequence							
Nucleic Acid Accession #: U92072							
Coding sequence: 351..3701							
15	1	11	21	31	41	51	
	GCGGGGCGAC	TGGCTGAGC	AGAGGCGGAG	CCCGGGGAGC	GCGGAGGGAC	TGCGGGGCTG	60
	CGGGTCATGG	ATCGCGCGC	AGCGGCGGAG	GGCGGCGGGA	GCCCGCGCCG	GACCAAGTGA	120
	GGAGGCGGCG	TCCGGGCGCA	CTCGAGCGGC	AGCGGCGCTG	GAGGAAAGAG	GCTCGCGCCG	180
20	GCGCGCGCGC	CGCGCGTCGC	TGCCCTCTCT	GTTGGGATTGA	TCTTCTGCTC	CCGCGTCTGT	240
	CTTGGCTGCC	GCGGGTCGAA	CGCGGCTCTA	GGCTTCAAGG	GCTGGGACTC	CTTGGCGAGCG	300
	GCGTCTCTCG	CTACCTGCGC	CTGTAGCTCG	GGGAGCCCTT	GGCGGAGACC	ATGAGGGAAT	360
	TCAATATGAG	GAGGTGGTGG	GAGGCTCTGA	CCCGAGGCTC	GTCTCTGGCT	TCCGACAGAG	420
	AGACACAGCA	GAGGACCGCG	CCTGGGAGCC	GGGAGCCCGA	GATCCAGGAG	AGCTCCAGGT	480
25	CCGAGCACTT	CCAACTCTCG	AAAGACTGTC	GCCATGGATT	TGCCATATCA	CGCTCCAGCC	540
	TGCGCTTTGA	TGCGGCTTCAG	AAAGTCTCTG	GCGTAGAGAC	CGAGACGGT	GCTTTAAGCG	600
	TCTTTTGTGG	TGCGAGGCTG	GAAATTTTAT	CGACGACAGA	CAAGCGAGG	CGATGATTCT	660
	AACTCCAGTT	CTGTATTAG	GAGGAGGCC	TCTTGAGTCC	CTTGCGTGA	GACACTCTAC	720
	ACTTGTGGAA	TTTACTCTAG	AAAGAGGCGT	CTGTGTCTCA	TTACTCTAAA	TTTTGCMAGG	780
30	AAAGGGTAC	ATTTGGCAAT	CTGCTCTTCC	AGAGTATGTT	GCTCTATGTC	GGACACGAGC	840
	GAGTATATAT	ACATCTGAGA	CAATGGCTAT	CGTCAAGCTA	CTCATATATG	CTCATATATG	900
	GGATTAAGCG	CATCGACATC	TGATCTAAAT	CTCACCCAGG	ACCTGTTGTC	CATATAGTGT	960
	ATATATCCAT	GGAGCGAGGG	AAAGCTCTGA	TGGGCTTTGA	ATCTGGACCA	GTAGTCTTAT	1020
	GGAGCTTTAA	CTGAAAGAGG	GCTGACTACA	GATACACTTA	GGACGAGGCT	ATTCACTCTG	1080
35	TGGCTTTGAA	TGCGAGGCTG	AAAGGTTTAT	TTTGAGCTAT	ACCTTATGCA	CTCATATATG	1140
	TATGGAGTGT	GAGCTCCCTC	ACTAAACCTG	TACAGACCAT	CACCTCTCAC	GGAAACAGAT	1200
	TAAAGATGGG	GAGAAACCC	GAGCCTGTGA	AGCCTATCTC	CAGGTGGGAG	TTCAGACAGT	1260
	CAGATGCGGG	GGAACTTTT	ATATATTTGT	CGGAGGCTCT	ATCATATGAT	ACCTTGGGAA	1320
	GAGAGCACTT	CTTTAGCAAT	ATGCATGAGC	ATGTGCTGGA	ATGACTATAT	ATGACTATAT	1380
	GAATTCCTCG	CTTCTCTACA	GAATGTGAAA	GGCCATATCC	AAATGATTAT	CAGACGCCCT	1440
	ATGCTGTGGT	TGTTCTCCCT	GAGAGGATT	TAGTGTCTAT	AGACTCTGCA	CAGATATGAT	1500
	ACCTCATATT	TGAGATATCC	TAOCTTTTGA	GTATACAGGA	GTGCCCTGTT	ACATGTTGTT	1560
	AAATATTTGC	TGATTTCTCT	GTGAGCTTTA	TCTCTGCACT	TTATTTCTGT	GGAGCTAGAG	1620
40	AGAAAGTCA	AGTTTACGCG	AAAGAGGAT	GGCCCATACA	TGTTGTTGAT	TGGGCTCTGG	1680
	GTGCTCAAG	TATCCACAGA	ATATATTTA	CAAGGCAATC	TGATGGCTCA	ATATTAATCT	1740
	GGATGCTCTC	TGCAATAAAT	CTACAGTAC	TGTATAAAAT	AAAGAACTCT	AAAGTATTTG	1800
	AAAGATCGAG	AAATATAAGT	GACAGCAGAG	ACACCGAGAT	TGTATAGTAA	GATCTCATAT	1860
	CAATTCAGAT	CATCTCTCTG	TGACAGAGAG	GCAGATATCT	GTTCATGCTC	CGAGTATGCT	1920
	CTCATCTCAT	CATTATATAG	TTCAGCAAGC	AGGAAATGCT	TACAGAAATC	ATCCCGATGC	1980
45	TTGAGATCCG	ACTGTATTAT	GAAATAAAT	ATTTGGAAAC	GCGGAGGGGT	GAGCAGCCAC	2040
	CCCTCTTCTC	CATCTCCCTG	GGAGCTCTCA	CGTCTCAAGC	CATCCCGCCCT	CAGTCTCAAT	2100
	CGTCTACAGG	CAGACAGCTCA	TGGGAGGGCG	TCTGAGAGCT	TTTACCGGTT	TTAAAGATTA	2160
	AAAGCTCAC	ACTTAAAGG	TCTCCCGCT	ATCCAAACGA	CGATGATGCT	CGATGATGCT	2220
	GGGTGGGTGG	AGAGACCGCG	CAGCAGATCA	CGAGCGTAGC	ACTCAACTCT	TCTTACGGAT	2280
50	TGTTGTGTTT	CGGCACTCC	AATGCGATTC	GAATGTTTGA	CTACTCTCAAG	AAAGCAGTCC	2340
	TGCTCAACTC	CAGACCAAT	GAACTATGCG	GCTCAATGCG	TGCTTATGCG	AGAGAACCGA	2400
	GCTTCCCGCT	CAATCTCTCG	CAGCTCTTGG	CGTGTGATAT	ACCGAGAGCA	ACCGAGAGCA	2460
	GCTGCTCCCG	AGAGATATCG	TGCAATATCT	CGACTCTCCG	AAAGATATCA	AGCAAAATTA	2520
	TGCTCCCAAC	TGATCTAAGG	CGTAGTTTAT	ATTTGAAAGG	CAATTCCTCT	ACGAGATATCT	2580
55	GGATTTGAGC	TGTGACCGAG	ATTGACAAGG	AGGCTCTTAT	AGGACTTTCT	GCTCTTCAAT	2640
	CTCTGTGAGC	CTTCCGAGAT	CGTCCGAGCT	CGTCCGAGCT	TGGGCGGGAG	TGGGCGGGAG	2700
	CCCAAGTGGG	AACTGCTCTT	GTATCAACGC	TGAATCTCCG	CTGSGGCGCT	GAGCAGAGAG	2760
	TGCTTCAAGC	AGTGAATGTT	TCTCCAGGCG	GTACTATATT	GAGTTTAAAA	GGTGGATGAT	2820
	TGAGATATGC	ATTTCGAGAT	GGCCGCGGCT	GCTTATATGC	ACCTGCATAC	GAACTCTGGA	2880
60	CAGAGCGGCT	CTTGAAGAGG	AAAGGAGGAA	ATTTGAAAGG	GGTGGAGGAG	GGTGGAGGAG	2940
	CTTCAAGTCT	CGCTCTCTCT	TCTCAAGGAA	TTAGTGAAGA	CGAGTATGCA	GTATATATTA	3000
	CTGAAGAGCA	AGCAAGATCT	ATTCATCTGC	CAACCCGAGA	CTGTGATAC	AAAGCAAGAA	3060
	TGACTGAGAG	GTCTCTCGTG	CTTCTGGGAG	ACATTTGTGC	CGTGGATTAAC	AGTGTCTGCC	3120
	TGCGCTGCTT	CTTGTCCGAG	GGCCAGATTA	TGACTCTTCA	TTTCCCGGAG	TGAGAGGCTC	3180
	TGCTGTGATAT	CGTCTCTCTA	CGCTTCTCTA	ACCTGAGGAG	CTTCTCTCTG	CTTCTCTCTG	3240
65	CGACAGTGGG	GGACAGCTTA	TACTCTTTT	CAGCTTCAAG	AATCCAGAGA	CTACACTACA	3300
	CTCAGGAGAG	GTGTGAAGAG	CTTCCGAGGA	TGCTTGTTGA	TCGCTTCAAC	CTGTAGAGAA	3360
	CACGCAAGAC	ACCAACAGGA	GGGTTCTTCT	AAAGCTTATT	TGAGAGTGGT	GCACATCTCT	3420
	TGATATAGGA	AGAGACTGTT	GAGAGTCTCT	CTCTGGGAAA	GGGCTCCAGG	AGCTTGGCAC	3480
70	AGCACTCCCG	GGGCTCTCGC	GGGATCGAGG	GTCTGGAGGG	AGCCCGGCTG	GGAGTGGTGG	3540
	GAGACTGGGC	CGGAGCGAGG	CTGCGCTCTG	ACGAAAGAGG	ACGAAAGTCT	AGTGAATCTG	3600
	AAAGAGGAGC	TGCGGCGTGG	AGTTCGAGTG	GAGACTGTTT	TTCCAAACAT	GCTCAAGAGC	3660
	TGATCTGAGA	ATAGACTGTT	ACGATTTCTG	ACAGATAGGA	CTCATAGAGT	CTCATAGAGT	3720
75	CCAGCTCTCA	CGACAGGAAA	AAAGACTCTT	CTTTTGTGAG	GTCACTATAT	TATTTGGGAA	3780
80	AGATAACATA	AAAGGAGTGC	ACACTGCTCA	CAGCGTCTCT	CCAGACAGCA	TCTGCACTT	

Seq ID NO: 21 Protein sequence
 Protein Accession #: AAD04756

WO 02/098358

PCT/US02/17594

```

1      11      21      31      41      51
5      MEKFNIRKVL DGLTAGSSSA SQQQQQQQHP PGNREPEIQE TLQSHFPLC KTVRGFPFYQ 60
      PRLAFAPDPQ KILAVGTQYTS ARLRGRKRCV SCTQMDHSGA AVIQQLPLN SGALVSALAD 120
      DTLELMLJLH KRNVLBLELS FGRKRVPTCH LPRQKRLVLT QTEKHCHVIT WVSFPLAGV 180
      VIMNKALELD SSKSHPGPVV HSKSNPMQEG KLLGFSESTQ VVLMDLKSKK KXYETVDEBA 240
      IHSVAKHHEG KQFICSHSDG TLTIMNVHPS TKPQVTITPH GEQLDKGKKP SPCKPIYLKVE 300
      FHTTRSGEPF LILSGSLSYD TVGRRPLCLV MEKSESTAVLE MDSIVDFLT LCETPYPHDF 360
      QEPYANVYLL EKDLVLIDLA QNSFIFPBP TPLSIESPV TCERYTADCE VOLTPALRSV 420
      GAGSGSGGTS KLEWPTDQSN WSLGAGGVFE IITGSHAGGS IKFWDA-SAIT AQLVTLKATS 480
      KVFESKSHKD DQKNTDIVDE DPAVQIISW CPBSKMLCIA GVSARHIVR PSKQSVTVTV 540
      IIMLVVELLY EIMDVETPEB EQPPPLSTPV GSTTSQIPPP QSHPTSSSS SDGLDNVPC 600
      LDKVNSLEQL SPQVQTELVLI QWVWGSSEP QITTSIALMS SVGLVWPSRS NGLTAMVTLQ 660
      KAVLNLNLTJ ELMDNPTYR SPKSPKPSKR POGAGLGGI TQTPVPSBR CKSPSMAHS 720
      RKLSLPTDLK POLDVKNPSF SRSRSSVTS IDKSEREALI ALHPCTFTFR KADSSPSFCL 780
      WVGTGTQTAI VITLMLPIAG BQRLQPVIV SPSTILALKI GAILRMAFID AAOCLMPPAY 840
      EPMTEHNVPE EKKKEKELKX HPFVSGSPSS SQHISBNQYA VICSEKQAV ISLPTQNCAY 900
      KQNTITSPFV LEEDIVLHSL SVCLACPCAN SHINTFSLP LKPLVLTPL PLZBNRLAKT 960
      FCFANSSGLD TVPTEYTOR LTVSQETCN IQBMLGELPT FVPEYEPAPR OFPKGLRQSG 1020
      AQSLEREELP GSESSGKASR SLAQHPPGP GIBGVGMAAS GVYZELARAR LAUDRGQGLK 1080
      SDLERTAAAM MSSADSPSKH AHMFLMKYD QXWYQF

```

Seq ID NO: 22 DNA sequence
Nucleic Acid Accession #: CAT cluster

```

1      11      21      31      41      51
30     TCCCATCGAG TGAAACCTGG TCTTGTTCCG TCGGCCACCA ATCCCTCTCC AGCTTTGACG 60
      GCCCCGGGCA AGCCTGGCTC GTTACAGCTC CTCTGCACCC TCGTGGAGCT TCAGCTCTCT 120
      CCGTTCACGA GAAGCTTATG GSGCACATCT GTTCGKCATC CGSGGGCGAG GTCCGCGGTS 180
      CGCCGGAGAG AAGAGAGPTR ACCTGGGGTT CTGACCCCG CTAACCCCG CTAACCCCG 240
      GTGCGCGCGC TCTTCAGGCG TCTGCTGGST CCCACTGBCG AGAGATTAGG TCTCAAGTCA 300
      GCGTAGGCTC CTGAGACGCC CAGGCCCGGA AAGACACGTA GGGGAACCA TCTGCTCACT 360
      TCTGCTCGTT CCGAGAGGGA TCCCTTCTCG ACGGGAAGA AGAGGCGTAA ACAAGACGTS 420
      TCGTCAAGAT AAGACCTCT GACCTGACCT CAGCTCAGCT ATTAACCTAA ACTGTAGAG 480
      CCGCTCCATC ACAGCGCTCA ACTACTGACT ACTGACGCT GACTGCTGT TCGTAGATT 540
      TTCTCTTGAT AAGAGACCACT TGGCCGTTGG CGSGTCTGTS ACGATTACA GAAGCATATG 600
      ACTTGATGCG CTTTGTGTCG CTGCTTCACC TTTTGAAAGA TAGGGCGCTAA TTATAGTGA 660
      TTTAAATGTT GTCTCCACCC CAAATGGAAC ATGGGTGSCA TGTAACAGGC ATGTATTACT 720
      AGCATGCGTG GACGAGGATC CTTTCAAGAA TATTCAGAG TCCCTTATC CCGTGTGAA 780
      TATGTATATG TGGCGACGCA GATCAAGTAA AATCACTATT CGCCCTCCCC TCCCTGGAAG 840
      CCACTATTTT GGGTGTCAAG AGAAGCTAT GCGTCCAGAG CTGTTCGAGG AGGGCCCAAT 900
      TTCGSGCTGS ATAGCCCTTT TATAAAAAAA TAAATATCTC TTTTAAATT TAAATATAGA 960
      CGCACACGAC GCGCTGACAC TATTGSGGPG GAAAGAGAT GAAAGAGAC GGTACTAGAT 1020
      TTGATGACCA TTTTGAAGGA GACAGGTGCG CCCAGGACAG CGACATCAC CAGTATACGA 1080
      GCTTAGACAT GCGGAGAGCG CGAGCGACTC ATAGACACAG ACAGCGCTCG CAAGCACCTA 1140
      AGCATAGCTA CTACACTCG TCGAAGAGATC ATACACAGAT TTCTATTGCG GA

```

Seq ID NO: 23 DNA sequence
Nucleic Acid Accession #: CAT cluster

```

1      11      21      31      41      51
55     CTATGAATCT CGGAATAATC TCAAACCATC AGCCTCTGCA AGAAGCAAG TGACAGGCCG 60
      GGGCGGGTGT CTGACTCTGT GAATCCCGAC ACTTTGGGAG CCGAGGTGTG CCGAGTACAG 120
      AGGTCHAGAG CTCTCAGACT TTCTGGCTAA ACCAGTGAAG CCCCTCTCT ACTAAAAAAA 180
      TGAAGAAAGC GATCTGATAC GAGTGTCTGC AGGAGAGAG CAGAAATGTA CAGTAAATGA 240
      GACCCAGGTA CACAGATGCA CGGCGGCCCC GCACACACAC ACNAGAGAA ATGAACCAAG 300
      AGGAAAGGAA ACAATTTCOA ATAAGCATTT GAGATGGGA AAAACACCTT GAACAGAAA 360
      TTCTAAAGAT ACGAATTTT TTTTAAAGTT AAAAAGGAA CAAATATAGA CAGAAATGTA 420
      ATGAATATAT AATATGTCTA TCGAATGTGA AGATATGTA AGGACAGGA AGGACAGGA 480
      GATCTAAATG CAAACTTAAG AAGGSGCAT TTTTATTTT TTTTATTTT AGACGCAACC 540
      TCACTCTGTC GC

```

Seq ID NO: 24 DNA sequence
Nucleic Acid Accession #: NM_000944.1
Coding sequence: 1115..3874

```

70     1      11      21      31      41      51
      CGAGATCCCG GGGAGCCAGC TTGCTGGGAG AGCGGAGACG TCCGAGACAA GCCCCAGGCG 60
      AGAGAGGCGC ACGAGGGGAA AAGGGGCCIA GCTAGCCGCT CCGATGCTGT ACAGAGGCCG 120
      AAGGAGGCGA CACAGCCAGC CGCAGCGCGG CTCACAGGAC AGCCAACTCC TCTTCCAGCG 180
      CGGSGGCTTC GAGGCGCTGT CCGTGGAGCT CCGTCTCTCT TCGGTGGAG TTTTAAAG 240
      CTCCTAAGAA CTCGAGAGGA GCAAGAGAA TGGCTGGTAG GACTGACGCG TGCTTTTCTC 300
      CTCCTCTCTCT CCGCCCGGCC TCCCTCCACC CTGCTCTCCC CCGTCCCCCC GCTCTCTCTCT 360
      CGCGAGCTGC CTTCAGTGGC TACTCTCAAC CAACCCCGCT CAGCACGCTT CTCCGACACC 420
      CGCTCCCCCG CCGCTCTCCG CCGAGCTCTG CAGCCCGAGT CAGCTAGGAG GTACTCTCT 480
      TTGCTCTGCA CGCGCGAGAC TAGCTCACAA TTGCAAGAA GCGCTCTAGG AGCCAGGCGA 540
      CTCGGGAGCG CTTCTAGCAC TGCGGCCGAG ACCCGCGTGG TTGAGATTCG GCGCGAGAGA 600
      AACCTCTGTT TCCGCCACTC CTCTCTCCAC CTGCTCTGCT CTTCGCCAGC CCGAGTGGCG 660
      ACAGAGATCT AAAAGTUAAG AAGGCGATCA GGTCTTCAAG AGCTCAAAA CAAAGCAAC 720

```

WO 02/098358

PCT/US02/17594

5
10
15
20
25
30
35
40
45
50
55
60

AAAAACAAAA AAGCCGAAAT AAAGAGAAAA GATAATAACT CAGTCTTTAT TTGCACCTAC 780
TTCAGTGGAC ACTGAATTGG GAAGGTGGAG GATTTTGTTT TTTCTCTTTA AGATCTGGGC 840
ATCTTTTGAA TCTACCTCTC AAGTATTAAG AGACAGACTG TGAACCTAGC AGGCAGATCT 900
TTGTCCACCG TGTTGTCTCT TCTCCACGAG ACITTTGAGG TGTTCAGAGC CTITT7TGGGT 960
GGTATCTGCT GCGATTATCT TCTCTGGAG CTCTCCCGAG GTGGGCACTT AGCTCTGAGT 1020
ACTACCTCAT CATACAGAGC TTGTGAAGCT TTCTGAGCA TTCTGAGGCA GAGCGAGGTA 1080
GGGAAGTAGT TGGGAAGTCT AGCCAGAGTC AAGGATGGAA GTGAGTATG GCTCTGGGAAG 1140
GTGTCACTCT CGCCGCTGCT CCAGAGACTA CCGAGAGAGT TCCGAGAACT TGTTCCAGAG 1200
CGTGGCGGAA GTATCTGAGA ACCCGGAGCA GACAGACCCA GAGCGCGGGA GCGACGACAC 1260
TCTCTGAGCT AGTGTGTGCT TGTCTGAGCA GCGAGGAGAG CAGGAGGAGC AGGACAGCA 1320
GGGTGAGGAT GTTCTCTCCC AAGCCCATCT TAGAGAGCCC ACMGCTACCC TGCTCTCGGA 1380
TAGAGACAGC CAACCTTTCAC AGCCGAGATC GGTCTGTGAG TGACACCCCG AGMAAGGTGT 1440
GTCTCCGAGC CTCTCCGAGC CCGTGGCCCG CAGAGAGGAG CTGCTCGGAC AGCTCGAGAG 1500
ACCTCGGAGC GAGGATGAAT CAGCTGCCCC ATCCAGGTGT TCCCTGTGCG GCCCCACTTT 1560
CCCCGGCTTA AGCAGCTGTCT CGCTGAACCT TAAGAGACAT CTGAGCGMGG CCAGCACCAT 1620
GCACTCTCTT CAGCAGACAG AGCGGAGAGC AGTATCCGAA GCGACGAGCA GCGGAGAGAG 1680
GAGGAGAGCC TGCGGGGCTCT CCACTCTCTT CAGAGACAT TACTGTAGGG GCACTCTGAG 1740
CATTTCTGAG AAGCCCAAGG AGTTGTGTAA GCGAGGTGCG GTGTCCATAG GCTGTGGTGT 1800
GGAGGGGTGT GAGCATCTGA GTCCAGGGGA ACAGCTTCCG GGGGATTCGA TGTAACGCC 1860
ACCTTTGGGA GTTCCACCGG CTGTGCTGCC CACTCTGTGT GCGCCATTGG CGGAATGCAA 1920
AGTGTCTCTT CTAGAGCGAC GCGCGGCGAA GAGCAGCTGA GATCTCTGCT AGTATTCGCC 2040
TTTCAAGGA GTTATACCA AAGCTCTTGA AGCGGAGAG CTATCTGTCT TGTCGAGC 2100
TGCGAGGAGG AGCTCCCGGA CACTTGAATC GCGCTTACCT CTGTCTCTCT ACAAGTCCGG 2160
AGCATCTGAC GAGCGAGCTCT CCGTCCGCTC TCGTCACTAC TACAACCTTC CACTGTGCTCT 2220
CGCGGAGAGC CGCGCCCTCT CCGCCGCTCT CAGTCCCCAC GCTCGCATAC AGCTGAGGAA 2280
CGCTCTGAGC TACGGGCTCT CCGTGGCGCC CAGTGTGCTC CAGTGTGCTC CAGTGTGCTC 2340
GGCGAGCGCT CTAGCGCGCG GTCTGAGCGG ACCCGGTCTC GCGTCACTCT CAGCGCCGCG 2400
TTCTCTCATC TGCGCAGCTC TCTTTCAGAG CAGAGAGAGC CAGTGTGTAT GACCTGTGG 2460
TGCTGTGTGG GTGTGTGTGG CGCGCGCGCG CGCGCGCGCG CGCGCGCGCG CGCGCGCGCG 2520
CGCGCGCGCG GAGAGAGAGC CTCTGAGCGC CTCTGAGCGC CTCTGAGCGC CTCTGAGCGC 2580
CGCGCGCGCG GAGAGAGAGC TCACTCGACCT TGAATGTGCG TACCCTGGCG CAGTGTGTGG 2640
CAGAGTCCGC TATCCCAAGT CCACTGTGTGT CAAGAAGCAA ATGGGCCCTT GAGTGTGATG 2700
CTATCTCGGA GATCTCGGCG ACATCGTGTG GAGAGCTGTT AGGAGACATG AGTGTGCCAT 2760
TGATCTGATG TTTCTGAGCT GTCTGAGCTG CTCTGAGCTG CTCTGAGCTG CTCTGAGCTG 2820
GACATAGAGA GCTCTCAGC GTGAGAGCTG CAGGTCTCTT TCCAAAGAG TCTGTGAAGG 2880
GAAGACAGAG TACCTGTGCG CCGACAGAAA TGACTGCAT ATTGAATAA TCCGAGAGGA 2940
AAGTGTCTGA TCTGTCTGCT TGTGAGAAAT TTATGAGACA GGGATGACTC TGCGAGCGCG 3000
GAGTCTGAGA AATCTTGATA GTCTGAACTT CAGAGAGGAA GGGAGAGGCT CAGCAGCAAC 3060
GAGCTCCCTC GAGAGAGACA CCGGAGAGCT CAGTGTGCTG CAGTGTGCTG CAGTGTGCTG 3120
TCAGCCCATC TTTCTGAAAT TCTTGAAGCG CATTTAGACA GGTGTAGTGT GTCTGTGACA 3180
CGACAAACAC CAGCCCGACT CTTTTCGAGC CTGTGCTCTG AGCTCAATG AACTGTGAGA 3240
GAGACAGCTG GTACAGTGGT TGAAGTGGCG CAGGCGCTTG CTGCGCTCTC GAGACTTACA 3300
CTTGAAGCAC CAGATGGCTC TACTCTGTA CTCTCGAGAG GGTCTGTGCT TGTGTGCAT 3360
GGGCTGGGGA TCGTTCACCA ATGTCAACTC CAGGATGCTC TACTCTGCTC CTATCTGTGT 3420
TTTCAATGAG TACCGCATGC ACAAGTCCCG GATGTACAGC CAGTGTGTCT GAGTAGGACA 3480
CTCTCTCTGA GAGTGTGAGT GGTCTCAAAAT CAGCCCGGAG GAATTCCTGT GAGTAGAAGC 3540
ACCTCTCTC TCAAGCTA TTTCAAGTGA TGGCTGTAA AATCAAAAT TCTTTGATGA 3600
ACTTCAAGAG AACTACATCA AGGACTCGA TCGTATCAT TCGTCAAAA GAATAAATCC 3660
CAGACTCTCG TCAAGAGCTC TCTACAGCT CACCAAGCTC CTGAGACTCG TGCGACTCAT 3720
TGCGAGAGAG CTGACTCAGT TCACTTTTGA CTTGCTTAAT AAGTCAACCA TGTTGAGCTGT 3780
GAGCTCTCGG GAGATGATGG CAGAGATCAT CTCTGTGCGA GCGCCGAGA TCTTCTGTGG 3840
GAGATTCAG CCGATTAATT TCCACACCA GCGAGCATCT GGAAGCCCTA TTTCTGACT 3900
CGAGCTCATG CCCCCTTCA GATGTCTCTC GCGTGTATA ACTCTGCACT ACTCTCTGCG 3960
AGTGCTTGG GGAATTTCTCT CTATGATGTG ACGTCTGTCT ATGAGACTGT TCTGTAATTCT 4020
TAGTGTGGCG GCTTTTCTCT TCTCTCTCTC TCTTCTCTCT TCTCTCTCTC CTCTCTATCT 4080
AAGCTCTCCA TGGCATCTCT AGACTCTGCT CAGTCTCTCT CAGTCTCTCT CAGTCTCTCT 4140
TGGTGTGGA TGCCTTAAA TCTGTATGCA TCTGTATGCA GCGCAAGTCT AAGTGTGTGT 4200
TGTCTACAGC ACTACTCTGT GCGAGCCACA CAAGCTTTA CTATCTTAT GCGACGGGAA 4260
GTTTAGAGAG CTAAAGTAT CTGGGGAAAT CAAGACAAA AACAGACAAA CAAGAAAAAA 4320
A

Seq ID NO: 25 Protein sequence
Protein Accession #: NP_000035.1

65
70
75
80

1 11 21 31 41 51
MIVQLGLGRV YTPKPKZTVR GAFNQLPQSV RVIQMPGPR IPFAGSAPFP GASLLLLQQQ 60
QDQDQDQDQ QDQDQDQDQ SPDQDQDQDQ SDGSPGABRR GPTFTVLDE HQDPSQDGA 120
LRCHIRHCH RCHIRHCH RCHIRHCH RCHIRHCH RCHIRHCH RCHIRHCH 180
DTLSBASTVO LQDQDQDQAV SBLSSSSRGR BASGAPTSSK DNYLGGTSTI DMARBLKCTA 240
VSVMSGLGYE ALRHLSPQBO LRGDQMYAPL LGVPPAVRFT PCAPLARCKG SLDDDSAGKS 300
TBTATSYSPF AGDFTVGLBG BSLGCSGBAA AGSSFTLRLP STLSLYRSGA LDRAAAYGR 360
DYNTFTLLA GPTFPPTPTP FALRLHLRPT LDVGSANRAA ANCRGQDIA GLICAGAGC 420
GSGSFAAAS SSMHTPLTAE EQGLYGPDCG GGGGCGGGGG GGGGCGGGGG GGGAGVAPLY 480
GYTFPPQGLA GDSDFPTAFD WYFPGMVSRR VFPSPCTVC SEMGPNWDSY GSPYDMLRL 540
TAGRDVLPIV YTFPQKTLK ICQDPSGCRG TQALTCGRC VYFKPABRER QYKLCASRND 600
CTIDFPRFRK CPKBLRATK BAKTLGARK TQDGLGARS GELGLGPTP PLESTGSLRL 660
VLSHIGTRCQ TPLNVLCAE ENPKVCAGHD HQCPDPSFAL LESLAELEGR QHVVYWKAC 720
ALDPFRLMIV DDQMAVIGYS WGLMVFMAK WRSTFVHNSR MLYFAPDLVF MYRMRKESRR 780
YBQCYRRLH SDRFQMLGT POEFLCMKAL KELSIPDVG LKRSIMVSDV RMNYTKLEDR 840
TACKRKNRP SCRRHRLGT KLDDSVQPIA RSLAQPTFDL LKRSIMVSDV PFRNMASTIS 900
VQVPLKLSK YKPIFRHQ

WO 02/098358

PCT/US02/17594

Seq ID NO: 26 DNA sequence

Nucleic Acid Accession #: CAT cluster

```

5      1      11      21      31      41      51
      |      |      |      |      |      |
      AGCATTTATCC ATGGCCAGTGT ATTGATGGAC TTCTTCAGGT CCTATGCAGA GTGCTTCATA 60
      TACTCTCATCT CAATCCCTCTA AATGAACCAAG AAAGTTCAGT ATATATCTCAT GTATACAGATG 120
      GAGGCTCAGAG AGGTGTTTAAAT TTTCGCCAGG TTCACAGTCT AGTAGTGTTT GNNNNNNNNH 180
      NNTGAAAGCTG TGTATATGCTG GTCTCAAGTC GATCTGTGTA TCTGTTGAC CAGATTTTGA 240
      ATAACTCTGTG ACTTTTCAGAG TATCCAGAGC GATTAAATAT AAOCCTTTGG TATAAATGTT 300
      CTCTCTCTCTG CTCTCTCTGTA ACAAATGGAG AAACAGAGTT CTACAAATAT TAAATATCAGC 360
      CTATAGACAGA GAGTATGTSAG AAATATATCTT TTTTATATAC AGAAGSTTCC CTATAGATCT 420
      TTTATGTTCTA TTTCAATATA AGCATTAACCT ATTGACATAT TTGCTGTCTA AGCGTGTCTT 480
      CTCGAGAAA AAAAAAANA AGTCGAC
  
```

Seq ID NO: 27 DNA sequence

Nucleic Acid Accession #: NM_006551.2

Coding sequence: 64...116

```

20     1      11      21      31      41      51
      |      |      |      |      |      |
      AATCTTAGAA GTCCAAATCA CTCATTGTCT GTGAAAGCTG AGCTCACAGC AAAACNAGCC 60
      ACGATGAGAC TGTGCTGTGTG TCTCTCTGTG GTCAAGCTCG CCCTCTCTGT CTACCAAGCC 120
      AATGCGAGAT TCTGCCCAAGC TCTTCTTTCT GAGCTGTTAG ACTTCTTCTT CATTAGTGAA 180
      CCTCTGTCTGA ACTTAAGTGC TCCCAAAATT TATGCCCTTC CGAAGCTGT TCAGCAAGAG 240
      TTAGAGATGA AGAGATGATC GATCAAGATG TCTCTCGAA AAGCAAGCTT CATGTCGAA 300
      GTCTCTGTGA AAATATTTGAA GAAATGTAGT TGTGTGACAT TAAAAACCTT CATCTGTGTT 360
      TCGACTGTCT TCTCAATGACA CCTGATCTTT CACTGCAGAA TGTAAAGTGT TCAGCTGCTT 420
      GCTTTAATAA ATCACTTGTCT CTAC
  
```

Seq ID NO: 28 Protein sequence

Protein Accession #: NP_006542.1

```

35     1      11      21      31      41      51
      |      |      |      |      |      |
      NELSVCLLLV TLALCCYQAN AEFCPALVSE LLEFFFIIEP LFKLSAKFPD APPEAVAAKL 60
      GVKRCTQDMS LQKRSLLIABV LVKLIKCSV
  
```

Seq ID NO: 29 DNA sequence

Nucleic Acid Accession #: NM_002645.1

Coding sequence: 1..5061

```

45     1      11      21      31      41      51
      |      |      |      |      |      |
      ATGCTCTAGA TATTAGCAA CAGCGGATTT AAAGAATGTC CATTTCACA TCGGAACCA 60
      ACAGAGACGA AAGATGTGGA CAAAGAGAAA GCAATACAGA TGGAGACAGA GGCTTAGTGA 120
      AAATCTGCAA ASGATAGACA AGTACATGAC AATCGAGAGG GCTTTAGTGT GTACAGAGC 180
      ACCGAAAAA AAGCAAGAGT TATATACAGC CAGACATATG ATCTCAAGGT GTTCTCTGAA 240
      TCGAGTTCCC AAAAAAGAGC ATTAGATATT GATGTAGAAA AGCTCAACCA AGCTGAACTT 300
      GAGAAACTAT TGTCTGATGA CAGTTTCGAG ACTAAAAA CACTGTATT ACCAGTTAG 360
      CCTATTGTA GGCCTTCTCT TTACACAGC ACTCATTTTA GACTACATAT TCAGAGAGGA 420
      CAGGCGCAC CTGATGTACC TGAGCTCTCC ACTATATCT TACTCTCTA TTATCTCTT 480
      ACTTACAGTA AACAGCTGTC ATCTCCAAAT GCTTCAATC CAGAAATGCC CACTTTTCCA 540
      TCGACGAAC CTATATATT AAATCTTCG GACAAATCTC CATATTTCTC ATATCTCTTG 600
      ACACCTGACA CAGCTTTTCA TCGACAGAGA AGCTTACTTA TCTATGTCAG AGTAGCAAG 660
      ACTGACATGT CAATACATCT TATCAAAATA CAGATGACAT CAGATTTT AAAAATATG 720
      AAAGCAGAGA CTGATTTTGA GATACAGAT TAAAGATCA GCACTACAGA GATATCTTCA 780
      AAGTCTGAGG ATATCAATTA TTTGACTGAG TTAGACTTGG ATCTCTAAG ATGCTCTAAG 840
      TGTATTAATG TGGAGTATTT AGACATGAG GAGAGAGAAA ATGTTTCAAG TTTCGTAGCA 900
      AAGATATCTT GAGATCTCTT TGAAGTCTGA GAGAGATGSA CAGCAATTT TCTCTGTGA 960
      AGAAAGTGA ATGAGAAATC CCTTCTGTG GMACTGTGA CAGAAAGCCA GTCTTTAAAT 1020
      ATTCAACACA CTGAGCTTGC AAAAGCCAG GGCCTATAT CTAGAGAGA CCCAAATGCG 1080
      ACGATATGTT TGCACACTGG AAGTCTCTCT CTTCAGAGAG TTAGAGTGA GATTAGAGAG 1140
      ATTGCAAGCT TTCTGTGATC CATTCAGAAA TGGAGACCA AATTTCADA TCCCAATGAC 1200
      CCAACAACCT CAGCATCTAT GTTAGTCTCA CTCAGAGCC AGAAGAACT ATGCGGAA 1260
      AATGCTAGTG TAAAGCTCTC CATGATCATT GAAGCATTC AGCTACCAAT TACTTTTAC 1320
      TGTGATGTA GTTCTACTGT AGAAATCAT ATATGCGAG CCTTTGCTG GTATCATGAT 1380
      GACTTGATCT AAGTAGATTT TGCATCATAT GTTCTAAGG TTGTGTCTA AGAGAAAGT 1440
      CTCTGAGATC ATATATGCTG TGAAGTCTCA GAGCATCTCT AAATCTGTG AAGATGAGC 1500
      ACAGAAATTA GACTCAATCT CTGAGCTTTC AGTGCAATG GTCAAAATCT GGCCGGAACA 1560
      GCGAGAGATG ATGAAACACCT CTTGATTTTA AACAAACAC TGTATCAAA AGAANAACCT 1620
      TCGACAGAG CAGTACAGAG AAGACCTTTT GAGCATCTCT TGATATCTTA TCACACCAA 1680
      GTGAGACTGT CTCTGATCTA TGAAGTCTCA CAGTACAGT TACATCAAT AATTAAGCT 1740
      GTAGAGAAA TCTGTATGTC TTAGATGCT GTCCAGACTC TTGCTCATAT AGATATCATA 1800
      AAGACGCTAA AAGAGCAGT TATCTTCCA AAGAGTAAAA CTGCTGATGT GACTTCTTTG 1860
      TTGTGAGAGG AAGACACTAG CAGGAGTTCA ACTAGAGGCT CACTTAATCT TGAATATCT 1920
      TTCTGATGTA GCAATATCTG GAGTATCTCA GCAATATCTG AGCTACAGCA 1980
      AATTTCTGTA GAGATCTTCA AGACTGTCTC TAGAGTGA AGATGTGAA GAGACATG 2040
      ACTACAGAG AGCAGCTCCA GTTACTATAT TTGCTGCTC ATGGAATTC AAGTAAATG 2100
      GTATCAATAT ATGAAATAAT CTCATGTGTA TGTTCACGCT CTCAATAGT AAAGATCTT 2160
      TTTAAACCTA TTCAATGAAA GAAGTGTGAC ACTTACAGAG ATTTCTTCTA TCTTATGAA 2220
      TGGATGAC TATCATTTT TCTGTCTGAG ATATCAATAT TGCATATGA ATCAGTTCTT 2280
  
```

WO 02/098358

PCT/US02/17594

CACCTTACCTC TTTTTGGAAAT TTAAATGAG AGCATGCGAA GTTCCCTCGA TTCTAATAG 3340
 CAGGAGAAGG GACCAAGAAGC TTATGGCGAA GTTCTCTTAC CTCTTGCGA CTTTAGACGG 2400
 1 TTTTACAT GTGAGCACTA ACTTCTATAT CTTTGACTT CATCRATAC AAATTCGTT 2460
 CTTGGAACAG TTACCAAAAG AGGATATGTC ATGGAAGAAG TAGTGCTACA GTGTGATTT 2520
 CTTCTCCGCG CATTTGATAT TATTATACCA ACTCCCTGAG TTGACAGAG CATTTACAG 2580
 CACCTTACCT TAGAACTACT AGAGATGAT ATAAAGGGA AACCTTCTGA TATTTCTAT 2640
 AAGAGCTACT CACTTGAGCT TTCTAAAGAA GATAAAGCTT TTTATAGGA GAACGTTAT 2700
 TATTGCTCTA AACACCCAAA TTGCTTCTC AAAATATTAG CAAGCGCCCC AAATCGGAAA 2760
 10 TGGGTGAATC TTGCGAAAGC TTATCCTATT CTTCACAGAG GCTCTGATAT GTACCACTA 2820
 ATTCCTGTG AGCTCTGGA TCTGAATATT CTTGATCGAG AGATGAGATC CTTAGCTGTG 2880
 CTTGAGATGG AGGCCATTTAG TCGATGATGAG CTAACAGATC TTCTTCCAGT GTTTGTAGCA 2940
 GOTTGAAAT ATGAHAATTTA CTTGAATAGT TCAATAGTGC AATTCCTTTT GTCGAGGCGA 3000
 TTGGAAGATA TCGAGATAGC AGCATATACA TATGTGCTTC TGAAGATGTC CTTGATGAT 3060
 15 GTACAGTTTA GTACAGTTTA CGAACHATTA TTGCTGCTTC TCTGTTCACT AGAGAGAAA 3120
 CGACTTAGAG AAGAGATCTT AAAACGAGC AACTCTGTAC AGCTTTTAGG AGGAGTAGCA 3180
 GAAHAAOTAA GCGAGGCTAG TGGATCAGCC AGACAGGTG TTCTCCAAAG AGTATGGAA 3240
 CGAGTACGAT CCTTTTCTTA GAAAAATAA TCGCGTCTCC CTCTACAGCC AGGCTTAGTG 3300
 GCAHAGAGAT TAAATATATA GTGTGCTCC CTCTTCAGTT CTAAGCTGCT CCCCTATAAA 3360
 20 GTTCAGAGG TGAATCTGA CTTCTGCGA GAGAAATTA ATGTCAAT TTAGGTGAGT 3420
 GAGATCTTC GCGAGATAT GTTAGCTTTA CAGATGATTA AGATATGGA TAAGATCTGG 3480
 CTTAAGAGAG GACTAGATCT GAGGATGATA ATTTCAAT TTCTCTCAAC TGGCAGAGAT 3540
 CGAGGCTGG TGGAGTGGT TCGTCTTCC GATGACCTTA GGAHAACTCA ATGTGATAT 3600
 GGTGTACAG GATCCTTTAA AGATATACC CTTGAGAGT TCTGAGGA ATACATGCT 3660
 25 TCTGAGAGAG AATATGAAGA GCTCTCAGAG AACTTATCT ATTCTGTGC TGGATCTGTG 3720
 GTGACCACT ATGTTTAAAG CATCTGTGAT GACACAGATG ACAATATAAT GTTCTGAAGC 3780
 ACGGAGACAA TGTTCACAC TACCTTTGGA AATTTTTCG GACATGACA GATGTGTGCG 3840
 ACTCTGAAA GGGATGAGC TCTTTTGTG CTGAGCTCTA AGTACGACA TGTACATAT 3900
 30 GGGGCTGAAA AGCCACCAAT TCGTTTCTG TTTTGTGCG ACCTCTGCTG TCGAGCTTAC 3960
 AACTTGATA GAAGCAGAC AAACCTTTT TCTAACCTCC TTCTCATGAT GATTCCTTCA 4020
 GGGTACAGG AACTTACAG TACTTCAAGT TCGAATAGAG TTAGAGATCC ACTCTCAACC 4080
 CACATACAG AGGATATTA TACATATTG TTCTACAGC TATTTGAATC AGCTTTGGA 4140
 35 ACGATCTGA CAAATGTTAA TCTCTCAT GCTACAGCTT CTGACCTGCT TTTTCTGAT 4200
 CTTCTCTGA ATATGAGCC CATCTCTCA TTTTCACTA AAACACTCTC CTTTAGACAA 4260
 GATGTGCGAA TCGAGGAAGT CTTCTTTT ACATATGTA AGAATATACA CCGAGATAAA 4320
 CATTAATAT AGGATATGCG AATTTGTGG GAGGAGACA TTGACCATCA ATTGTCTTCT 4380
 40 CGAACTATG TGAATCTGA CGAACTGAC TACTATATT TCGCTTCTG TTTTCTGAT 4440
 AAGTATACG AGCTTCTTAA TAGATGATCT CTAAGAGAA CACATATAA AGATGTATCA 4500
 GCGAAAGGA AAAATGAGT AAAACAGT TCGAGAGT TGAATGATCC TTCAACGAT 4560
 45 GTAGACAGT GTAGATCTTG TTGACTTTC TCTCACGCT TACTGTGTA TAGAAGACT 4620
 GAGAGGCTG CTAGCTTGA AGTACGAGT TCTCTCAT CTCTACGAG AGCTTACAGA 4680
 GAGGCTGTGA AATATCTAT CTTTACGGA AATGTACTCT TTTTCACTAT GTGTATGCT 4740
 ATCAAGATC TTGTTACTGA AGATGAGCT GACCCAAATC CATATGTGA AACATACCTA 4800
 CTTCCAGATA ACCACAAAC ATCCAAAGT AAACCAAAA TTTCAGAAA AGCAGAGAT 4860
 50 CGGACATTA ATGAATCTT TGTATGAGT GAGATGACT AAGAAAGCT AGGACAGCA 4920
 45 GAACCTCAAC TAGGTACT CAGTSCAGAA TCTCTGCGG AGAATTTT CTTGTGTGA 4980
 GTAAACCTCG CTTGAAAGA TTTCAGCTG AGCAHAGA CCGTAAATG GTATCAGCT 5040
 ACTCGGCGCA CATACTGTA A

Seq ID NO: 30 Protein sequence
 Protein Accession #: WP_002636.1

1 11 21 31 41 51
 | | | | |
 55 MAQIPNSGF KECPPGHPET TRAKDVKEE ALQMEARLA KLQKDRQVTD MQRGFELESG 60
 TKKXQVYKQ QYDMLVFFE SDQKRALDI DVSKLTQABL IKLLLDSPSE TKCTPVLEVT 120
 PILSPSFAQ DYFKEPTIQG QWPPGLDPS TIALPSITPS TYSKQAPFN GPMPHEPFT 180
 STEFVLESL QGQVPSYFL TATPRPQD SLVTPVLEP LMALEPKDI ASTSPFLAK 240
 KARTOLEIT SKVNSVLEP KSEDISKFPN LQDPLSEPK VDNVSVLOHE ERIAVSGLLA 300
 60 KIDPWAVILLE ERSTACHLE SKVHKSLSLV ATYTRSQSLM IETQLAKAQ GHISQKDNKG 360
 TBSLPTGSEL LQEVQVQHE MNAPCRATK LTKFPFVPH KNPQVLLP KNPQVLLP 420
 NAGVKEVIDI EGFGLPVFT NVGSEVTEI IMQALCWED DLNQVTVGSL PLACVQGEV 480
 LQNNLKGSH EHLQKQMD TRLKQLQFT GMCKQWAK AGDTPVTL MHLVLEIEP 540
 CIEAMTEKPEV EELDDYHQV VELAQLIHM BRAVDQVKA VKIKTSALDG VTEIATIESV 600
 65 KIKLRANVLP RSTADVTSL PGGEDTSRS TROSLMPNP VQVSIQTLA AIYDLRLHA 660
 NSRGSPDCA QSRKSVKZAM TTTELQPTI FANGGISENV NVNTKXTLL CSEHSEKDL 720
 PFIQSPDCA QSRKSVYLLK WEELITPFI ELPLPSEVL HTLPLPGLK ASTSPFLAK 780
 QEKPELALG VSLPLCFRFL PLTCSTGLLY LWTSESTMSV PCTVTKGVV MERIVLQVF 840
 70 PEPAFDIIT TPQVDSRIQ QHMLSTLEND IKKLLDLIL KDSSILGSKS DKAFLEWRY 860
 YCKEIPNCLP KILASAPMK KGNLRYTSL LHMPLVPL IALHLDSEK ADPWRKSLV 920
 THBAIDATG LTLMLPQV ALVETVLSL KMLLETPLM LQNTGIMBL TWLEDALEH 980
 75 VQFSTRYHV LQALLPVQK RLRESLQKT KJVLQGVGA ENVRQAGSGA QVRLQSRME 1040
 RVQSPFNKX CRPLKPSLV AKRLNIKSCS PFSNNAVLK VTNVWADPLG EELNVMPKGV 1100
 EDLQDMLAL QIKIKIDKLV LKSLDLRWV IFCLSTGRD RNVSLVPAV DTLKIQEY 1160
 80 VQVQKQVQD LARKEVLEK SEHSEVAGE HFYSCMCK VATTVLGCT RHMMDILAS 1220
 TGNPHIDG KFLGHAQMG SPKRKNAPPV ITCMNAVIN GSEKPTIRP LPVLQCTAY 1280
 NLIRKQTNPL LALLSLMIPS GLPVLSTIG LKVRDALQP QTTDAEATF PTRLIESLIG 1340
 SIATKPMFFI IMLAQLEFQV LPSNDEPLS FSKPTYSER DRIKEVSVY TYIRKINDEK 1400
 HYIVVKILM EQLLEPSPV KVFVSQRLH KMLLETPLM KLPFPPHAK LKTHLEKDA 1460
 85 ARKTRASTY LQRLWQMD VARDLQCTP PHLDLAKA ERIASERAG SFSPQTLG 1520
 GAVKLSYR NQTLFTMHVI IEDLVTEGA DMPEYVCTV LPMHRTSRV KTKISRTN 1580
 PTFNMLVYS GYSKELMBR ELQSLVLSAS SLKRNFFLAG VLPLKDFHL KRTVTKQVL 1640
 TAATTL

PCT/US02/17594

Nucleic Acid Accession #: CAT cluster

Seq ID NO: 32	RNA sequence	Nucleic Acid Accession #	CAT cluster				
1	11	21	31	41	51		
1	CAGTCAGATT	TTCTTTTGGC	TACGACAAAG	CAAGAGCGAT	TACTTACGCT	GAGCGCAUAT	60
2	CGATGTCGAT	CGAGGACGCG	CGAGGACGCG	CGAGGACGCG	CGAGGACGCG	CGAGGACGCG	120
3	GATTTTCAAT	TTCTTTTGGC	TACGACAAAG	CAAGAGCGAT	TACTTACGCT	GAGCGCAUAT	180
4	GATTTTCAAT	TTCTTTTGGC	TACGACAAAG	CAAGAGCGAT	TACTTACGCT	GAGCGCAUAT	240
5	GOCACAGAAA	TTCTTTTGGC	TACGACAAAG	CAAGAGCGAT	TACTTACGCT	GAGCGCAUAT	300
6	CGTCAGATTA	TTCTTTTGGC	TACGACAAAG	CAAGAGCGAT	TACTTACGCT	GAGCGCAUAT	360
7	CGTCAGATTA	TTCTTTTGGC	TACGACAAAG	CAAGAGCGAT	TACTTACGCT	GAGCGCAUAT	420
8	CGTCAGATTA	TTCTTTTGGC	TACGACAAAG	CAAGAGCGAT	TACTTACGCT	GAGCGCAUAT	480
9	CGTCAGATTA	TTCTTTTGGC	TACGACAAAG	CAAGAGCGAT	TACTTACGCT	GAGCGCAUAT	540
10	CGTCAGATTA	TTCTTTTGGC	TACGACAAAG	CAAGAGCGAT	TACTTACGCT	GAGCGCAUAT	600
11	CGTCAGATTA	TTCTTTTGGC	TACGACAAAG	CAAGAGCGAT	TACTTACGCT	GAGCGCAUAT	660
12	CGTCAGATTA	TTCTTTTGGC	TACGACAAAG	CAAGAGCGAT	TACTTACGCT	GAGCGCAUAT	720
13	CGTCAGATTA	TTCTTTTGGC	TACGACAAAG	CAAGAGCGAT	TACTTACGCT	GAGCGCAUAT	780
14	CGTCAGATTA	TTCTTTTGGC	TACGACAAAG	CAAGAGCGAT	TACTTACGCT	GAGCGCAUAT	840
15	CGTCAGATTA	TTCTTTTGGC	TACGACAAAG	CAAGAGCGAT	TACTTACGCT	GAGCGCAUAT	900
16	CGTCAGATTA	TTCTTTTGGC	TACGACAAAG	CAAGAGCGAT	TACTTACGCT	GAGCGCAUAT	960
17	CGTCAGATTA	TTCTTTTGGC	TACGACAAAG	CAAGAGCGAT	TACTTACGCT	GAGCGCAUAT	1020
18	CGTCAGATTA	TTCTTTTGGC	TACGACAAAG	CAAGAGCGAT	TACTTACGCT	GAGCGCAUAT	1080
19	CGTCAGATTA	TTCTTTTGGC	TACGACAAAG	CAAGAGCGAT	TACTTACGCT	GAGCGCAUAT	1140
20	CGTCAGATTA	TTCTTTTGGC	TACGACAAAG	CAAGAGCGAT	TACTTACGCT	GAGCGCAUAT	1200
21	CGTCAGATTA	TTCTTTTGGC	TACGACAAAG	CAAGAGCGAT	TACTTACGCT	GAGCGCAUAT	1260
22	CGTCAGATTA	TTCTTTTGGC	TACGACAAAG	CAAGAGCGAT	TACTTACGCT	GAGCGCAUAT	1320
23	CGTCAGATTA	TTCTTTTGGC	TACGACAAAG	CAAGAGCGAT	TACTTACGCT	GAGCGCAUAT	1380
24	CGTCAGATTA	TTCTTTTGGC	TACGACAAAG	CAAGAGCGAT	TACTTACGCT	GAGCGCAUAT	1440
25	CGTCAGATTA	TTCTTTTGGC	TACGACAAAG	CAAGAGCGAT	TACTTACGCT	GAGCGCAUAT	1500
26	CGTCAGATTA	TTCTTTTGGC	TACGACAAAG	CAAGAGCGAT	TACTTACGCT	GAGCGCAUAT	1560
27	CGTCAGATTA	TTCTTTTGGC	TACGACAAAG	CAAGAGCGAT	TACTTACGCT	GAGCGCAUAT	1620
28	CGTCAGATTA	TTCTTTTGGC	TACGACAAAG	CAAGAGCGAT	TACTTACGCT	GAGCGCAUAT	1680
29	CGTCAGATTA	TTCTTTTGGC	TACGACAAAG	CAAGAGCGAT	TACTTACGCT	GAGCGCAUAT	1740
30	CGTCAGATTA	TTCTTTTGGC	TACGACAAAG	CAAGAGCGAT	TACTTACGCT	GAGCGCAUAT	1800
31	CGTCAGATTA	TTCTTTTGGC	TACGACAAAG	CAAGAGCGAT	TACTTACGCT	GAGCGCAUAT	1860
32	CGTCAGATTA	TTCTTTTGGC	TACGACAAAG	CAAGAGCGAT	TACTTACGCT	GAGCGCAUAT	1920
33	CGTCAGATTA	TTCTTTTGGC	TACGACAAAG	CAAGAGCGAT	TACTTACGCT	GAGCGCAUAT	1980
34	CGTCAGATTA	TTCTTTTGGC	TACGACAAAG	CAAGAGCGAT	TACTTACGCT	GAGCGCAUAT	2040
35	CGTCAGATTA	TTCTTTTGGC	TACGACAAAG	CAAGAGCGAT	TACTTACGCT	GAGCGCAUAT	2100
36	CGTCAGATTA	TTCTTTTGGC	TACGACAAAG	CAAGAGCGAT	TACTTACGCT	GAGCGCAUAT	2160
37	CGTCAGATTA	TTCTTTTGGC	TACGACAAAG	CAAGAGCGAT	TACTTACGCT	GAGCGCAUAT	2220
38	CGTCAGATTA	TTCTTTTGGC	TACGACAAAG	CAAGAGCGAT	TACTTACGCT	GAGCGCAUAT	2280
39	CGTCAGATTA	TTCTTTTGGC	TACGACAAAG	CAAGAGCGAT	TACTTACGCT	GAGCGCAUAT	2340
40	CGTCAGATTA	TTCTTTTGGC	TACGACAAAG	CAAGAGCGAT	TACTTACGCT	GAGCGCAUAT	2400
41	CGTCAGATTA	TTCTTTTGGC	TACGACAAAG	CAAGAGCGAT	TACTTACGCT	GAGCGCAUAT	2460
42	CGTCAGATTA	TTCTTTTGGC	TACGACAAAG	CAAGAGCGAT	TACTTACGCT	GAGCGCAUAT	2520
43	CGTCAGATTA	TTCTTTTGGC	TACGACAAAG	CAAGAGCGAT	TACTTACGCT	GAGCGCAUAT	2580
44	CGTCAGATTA	TTCTTTTGGC	TACGACAA				

Seq ID NO: 33 DNA sequence
Nucleic Acid Accession #: AK026418.1

Seq ID NO: 34 DNA sequence
Nucleic Acid Accession #s: CAT cluster

1	11	21	31	41	51	
75	CTCATCTAATA	GGTGGCGGCC	GCTGTGCTG	TTTTTTTTT	TGTCGTCTG	TTCTCATCTAA
	CGACGTCTGCT	AGTCTCTCTG	CTGCTCTGGA	GTCTCTCTGA	GTCTCTCTGA	GTCTCTCTGA
	ATGTTGGTCTG	AGTGGTCTCT	CTCATCTAAT	CTGCTCTGTC	CTGCTCTGTC	CTGCTCTGTC
	CAATCTGGTT	TGAATTAATG	ATATTAATAG	TATATTAATG	GAAATTAATG	CTAGCTCTGA
80	AATCTCTGCT	TCTATCTCTC	ATACACCTCA	ATCAGGAAAT	CGACGCAAT	CTTCGCTCTG
	TATCTATGAA	CTGCTCTCTG	CTGCTCTCTG	ATCTCTCTGA	AAGCTCTCTG	CTCTCTCTCT
	ACGCAATCTG	TAATCTATGA	ATGATCTAAT	TAGCTCTCTG	TTTAAATCTG	ATATGCTCTG
	ATATGACAGA	TAATCATGAA	ATGATCTGAG	ACAAATAGAG	TTCTCAAGTT	CTAGCTCTCTA
						CTAGCTCTCTA

WO 02/098358

PCT/US02/17594

ATACAGCCAT GTCCAGGCGC GATGGAAATT ATGCGGGGAAT ATCCAAATTA GATACACGCT 600
GCCGATCGCC CCGGTTATAA TAATACAGGT TTATATATGA CMAATCCACA TCTTGGTTTA

Seq ID NO: 35 DNA sequence
Nucleic Acid Accession #: NM_018490.1
Coding sequence: 445..3306

1 11 21 31 41 51
10 CCGCGGCTGG GAGACAGCGA GCGGAGGCTT GCGTGTCTTG GCGAGAGCCA GCGCGGGGCG 60
TGGGGCGAGT GCGCGGCGAT GCTCAAGGCT GCGCTCTGCA ACCTTGAGGA GCGCGTCGAT 120
TGAGAGGCCA GGGACAGGGA GACCGGTGCG ATCGCGAGAG GCGGCGCCCG CCGCTGCGGC 180
GGCGCGCGCC GCGTGGCGCT GAGCGCGGGA GGAAGCGGGG TGCGCTTGCG GCGTCACAGA 240
GACAGCGGAA GGGCGAAACT CCGGAGCGCC GCGTCCCGCC GCGCGCTGGG GCGACTCTCG 300
15 AGCGGGCCGA GCGCGCGGAT ACCTCCGAGG AGAGCGAGCC GCGTCCCGGA GCGCGGCGCG 360
CTGCGCGGGG GCGCGCGGGG AGCTCGAGAG GCGAGCGAGG GAGCAGCGCC GCGGAGAGGG 420
CGCGCGCGGG AGCGCGCGCG AGCAATGCGG GCGCGCGTAG GCGTCTCTGG CTTCCTCGCG 480
CTGCGGCTGG TCGGCTGGCG GCGGCGCGAG GCGCGCGGCG GCGCTCTCTG GCGCGCGGCC 540
TGCGGCTGG AGCGGAGGCG TGCGTGTGAG TGCTTCGGGA AGGCGGTGAC GCGCGTGGCC 600
20 GAGGCGCTCA GCGCGCTCAC CCGAGCGCTG GATATCAATG TGAACACATC TACTCACTTG 660
CCGAAAGATG CATTATAGAA CTTCTCTTTT CTAGAGAGC TACAATTGGC GCGCAACGAC 720
CTTTCTTTTA TCAACCCAAA GGCGCTGTCT GGGTTGAAGG AATCCAAAGT TCTAACGCTC 780
GGAATAATC AGTTGAAGAC AGTACCCAGT GAGGCCATTC GAGGCGTAGG TGCTTGTGAG 840
TCTTGTGTTT TATATGCCA CCGATATCAC TGATCTCCCG AGCACAGTTT TGAGAGCATC 900
25 GTTCGATGAC GGCATCTGTG GCTGGATGAC AACAGCTTGA CGGAGGTGCC TGTCGACCC 960
CTCGACATTC TGCCGCCCTT ACAAGCGGCT ACCCTGGCTC TCAACAGATC CTCGAGCATC 1020
CTCGACTCTG CATTTCAGCA CTTTTCAGCG CTCTGTGAGT TGACATCTCA TACACATATA 1080
ATTAGAGGCT TGCGTCCGCA CTTTCTTGAT GGCATGATA ACCTCGAGC CTCACACTT 1140
AGTTATATA ACTTGGGGGA GCTCTCTCAG GCTATTAAAG CCGCTCTAGC CTTTAAAGAG 1200
30 CTGAGATTTT ATAGTATATC TATTCTGTGT ATCCCTGATG GAGCATTTGA TGATATACTA 1260
CTCTTAGAAA CTATACATTT GATATATATC CTCTGTCTCT TTGTGCGGAA CTCAGCATCT 1320
CGATATAT CTATCTGATG TCTCTGATGT ATCTGTGTGT TGATGAGTGT GACGAGTTC 1380
CCCATCTTA CAGAGACTGT CCACCTGGAA AGTCTGACT TGACGAGTAC AAGATATAGC 1440
AGCATACCTA ATAAATTTTG TGAGAAACAA AGATGCTTTA GGCATTTGGA CTTGTCTTCA 1500
35 AATATATATA GAGACCTTCC AAGTTTAAAT GGTTCGCAAT CTCGCGAGGA AATTTCCTTA 1560
CAGCTGTAT AAGTATAGCA AATATAGGAA GAGACCTCTC AAGCTCTGAT GCTCTTAGAG 1620
ATCTTAGATG GTTCTAGAAA CCGTAGATAC GAAATTCACA GTAGAGCTTT TGCCCATCTT 1680
GGGCAATATA CTAACTCAGA TGAAGTTTTC AATGAAATTA CTTCTTCC TCAGGAGGCG 1740
CGAATGGGCG TAATCTACT GAAACTGTGT GGCACATCTCA AGCTGAAGAA AGCCTTAGCA 1800
40 GGAAGAGCT GTTCTAACTT CAGCTCTTTA TGCGTAGGTC ATGCTATACA GATCTCTTCA 1860
TTTCTGCTC GTGCTCAATG TCTCAACTAT AACAAGAGG AACACAGAG CAGAGCTACA 1920
AGTGTGTGAC AGAGAGAGAG TACTCTGATG GCGAGCAATG TCACAGACAC CTTTGAATAT 1980
GAGAACATA CTGAATATAT TATCCTGTCT ACACCTCTCA CAGTGTCTTT TAAGCGCTGT 2040
45 GAATATTAC TGGGAGGCTG GATGATTGCT CTATCGTGCT GGTTCATTTT CTGTGTGCA 2100
TATTTTCA ACCTCTGT TATTTTAA CAATCTGAT CTGTATAT CACTGCTCTG 2160
TCCAAATGT TTATAGGCTT GATTCTGTG TCTAACATAT TCAATGGAA CTATACTGCG 2220
ATCTCAACTT TCTCTGATCG TGCTGCTGG GCGAGATTGG CTGAATTTGG CATTGTGGTG 2280
GAAACTGGCA GTGCGTGGCA AGTAGCTGAG TTCTTGTGCG TTTTCTCCCT AGAATAGGCT 2340
50 AATTTTTAT TAATCTGAG AACTGTGGA AGAGCTTAT CTGCAAGAA TATATAGAAA 2400
AATGGGAGA GCAATCATCT CAACAGTTCC CGGTTCTGCT CCGTTTCCGC TTTCAGGTCT 2460
GCTACATGAG CAGCTGATT TCCCTTTTTC CATAGAGGGG AATATTCTGC ATCACCCCTT 2520
TTTGTGCAAT TCTCTACAGG TGAACCGGCA CCAATAGAGT TCACCTPACCT OTTAGTGCTA 2580
TAAAGTAC TACGATTTT ATATAGGCC GTATCTACCA CTAGAGCTAT CCGACAGTG 2640
55 GAAAGAGAG ACCCTCTGGA AATCTCAACA TCAAGCATGT CTTCTGTGCTA CTTCTGTGCT 2700
ATCTTACCA ATTCGATCTT TTTCTGCGCT GTGGCGTTTT TTTCAATTCG ACCATATGAT 2760
ACTCGAATCT CTACGAGCGC GGAATATAGT AAGTCTGTTA CTCGTGATAT TTTTCCATCT 2820
CTGCTGTGCT TGAGTCAAGT CCGTGAATTT TTCTCAACG CAAGGTTTAA AGAGAGCTGG 2880
AAGTATCTA AGCACTGCT TCCACAGAAA ATGTGATGAT TTTCTATTC CATCTGATG 2940
GAGAGTGGT GTCTGAGACA GAAATTTCTAC TAGACCTGTG GCAATGTACT ACAATTCAG 3000
60 CGGACCTGCA CTTGTTGCGA CTGCTGCGAA TGTTTTCTTT TAACAAAGCG AGTATCATGC 3060
AACAACCTGA TAAATACACA CAGCTCTGCT GAGTGTGAGT TGCTCTCTTG CCGAAGAGCT 3120
GAGGCGATCT GGTGCGATCT TGCGGCGGCT TGCGGCGGCT CTGTATCTA AGTGTGAGT 3180
GATCTCTCTG TCTGAGCAGG TTCTGACAGG GTGAGCGGCT GTGAGGAGC GCTCTCTAC 3240
CAGAGTAGAG GATTCGCGAT GTGGGCGTAT GCTTCAACTC TACCAGAGT TAAGAGAGCT 3300
65 ACTCATGCTT GGTACACGCT TTCCCGGCTC AACCAAAAT AGTGTTATA GAGTGAAGCC 3360
TATCTGACA TTCTCTGCTT GAGACGCTTG GCGGCTGTGT ACTATAGAG 3420
AGGAGAGGTT GCAATTTAAT TCTCAACACA GTCAATTTCA AAGACAGGT GCTCAAAATA 3480
TAAATTTGTT AAAATAGCAA TGTCAAGCA ATGTATGATC TGTTTGAAAC AATATATGA 3540
CTGAAAAGG ATCTTAGGTT TAGATGAGCA ATATATGAT AGTTTTCCT GATCATATAG 3600
70 AAGCAAATTT ATACCTATTT TGATATTAAG CACAGAGATA AAGACAGCTG TTATATATCT 3660
TTAAATATCT ATTTGAATTT GGAATTTCT ATACAGAG AAGATATCTT GCTAATTTA 3720
CCTAATTTT CATCTTAAT CTACAGACAA CTATCTGCG GCGCAAAAA GCGACTGTCC 3780
CAGCTAGAAC TGTAGAGCTA TACATAGCA TTACTTAAT ATGTTTTAC TTGCATCTC 3840
TGACATAGA GAATATATA TTTTGTTTA GCAATTTATA AATCAAAAC CTGAGATCT 3900
75 TTTTAAAGC GTTCTAGC CTGTGAGT TGAATAATG CTGGAGATCT GTTCTACAG 3960
ATTATACAT CTTTGTGCTC AATCAATAT TTTTCTTGA GTTGTTTGZ ATTACACATC 4020
TGAAAAAAA GTTAAAGGCT AATTCGTGTT TGCTTTIAGT CGATTGTGCT AATCATCA 4080
CTAATGTGGG GPTAATATAG TATCTAGGG ATTTGTGGG TCGAGTAAT GTTTCATTA 4140
ATGATATCT CTAATATCT TGCTCTCTAC TAAATATTT CAACTGTCT GATATCTA 4200
80 TAGCAATGCT TTGAGATTAA TAGAAGTAA ACTGTGCTCA ATACTTCACT TTAATATAG 4260
GAAACGGGGA CTAATATAGA CAGAGATGAC TTATGTTTAT TTCTATGUA GCTGGATATC 4320
CTGGAACCTG TGCTATATA TGAATAATTC CATACATCTT CCGCACTATA TTTTATATA 4380
AAGAGCTAT TCAATAGCTC AGAGGCTGGA CTCTGCTTAA CAGAGTAAT ATTATATTA 4440

WO 02/098358

PCT/US02/17594

TAAAAATAGA AGAAGAAGAA ATAAAGCTTA GTCCTGGGTC TTTAAAAATT AAAAATTTTA 4506
 CTTAATGCC ABATAGAGCA ATAGAGCTA TACCTGTAAA GTATATAGTA 4560
 TCCATATGCT TTTTGAACA GTATGCTAAA TCAATAGCAA ACCCACTGCC ATTATGTTA 4620
 TCTGAATATC ACTAAAAAAA TCCAGCTAGC TGTCAAGTTTA ATAAATAAAC TCCATACT 4680
 TCCATATAAA TGAATTTTTA TCTATATGTA ATATATTTTA GAACAACAAG TGGAAATAT 4740
 GCTCTCTGTC CAGCTGCTCT AATATAAGCT ACTCTCCAGA CTAGAGTGGC TGGACATG 4800
 AGACTGTAAA ATGTGCTGTT ATACATCTTT TGCATTTGTA ATACNTGTC TGTACATG 4860
 TCACTTTAAT AAAACAGAAA TCTTTTGATA TCAAAATCAT GTAGTTGTA TAAATGTGG 4920
 GAAGATTTTA TTTACATGTT GTTGTAAATT TGTAGAGGCC ACATATTACA AGTTTAAAA 4980
 ATCTCATCTA TGTATATTTA CAATCTGAT AAATATPAAA TONTAACTG GTAGGAACCT 5040
 CTTAACTAAA AGTCTCTG CAAATTTGCG GTATATGAAA ATTCTTCTT TTTATCTATT 5100
 AAAAATCAGA ATAAACAGCA TATAAAGTGT TTAATCTTGT TGTCTATGCG TATGAATAC 5160
 AATATGTGAC TCACTGTTT GAATTATTTA AGTTTCTAGA AAGCAAAAAA A

Seq ID NO: 36 Protein sequence
 Protein Accession #: NP_060960.1

1 11 21 31 41 51
 | | | | |
 20 MPGLGLLCLF LAQLGLGAG PSGAAPFLCA APCSCGDGRK VDCGCKGLTA VPGLLSAFTQ 60
 ALDISGNMT QLPEDAFNFP FLBELQLQAG NDLSPHFKFA LGLKLEKLV TLQNNQLKTV 120
 PSBAIRGLGA LQSLRLDAHH ITSPVEDSFE GLVQLRLWLH DGNLSUVEVP HPLSNLPLAQ 180
 ALTLAKIS SIPOFAPNHL SSVLVRLAHN NKIRLSQHC FGLDLHLEL DLSIHLGEP 240
 PQAHLRSL KGLGPHRSI GTPDGAFQ NPLRLTHLY DNLSPVDS ASSLNLSLHS 300
 25 LVIRKASVP QFNHLTGVTH LMSLTGVTGT ISSIPLNQLQ EQDMLRLDL SYNIRDLHS 360
 FNGCHALERI SLQRPHYIQI KSTPQGLIS LAILOLSNLH IHEHSRAFA TLGPIINLGV 420
 SPHELSTPT EBSHSLMLK LUGSPFLKBA LAAPDFMLR SLVPTVLT CT CPWFGLSDA 480
 HLTEDHNGI DHPVAGHGT ADANATPTG BHEHAGHII ICTPTGTH ICTPTGTH 540
 IRLTVNFIPL VALFNLNLI LTTVAFTSL PSKFLIGLI SVSNLPMIY TGLITFLDAV 600
 30 SWGRFAEPGI WNETGSGCKV AGPLAVFSSE SAIFLMLAT VERSLSKADI NMGKSHLKL 660
 QPFWALSAEP LKATVACQFP LPHREYVAS PLCLPFPFGE TFSIGPTVTL VLAHSLAVLL 720
 NAVITYELIC NLKELSELN GSHSLKETA WLTPNCFIF CFVAFPSAPR LITATISLSP 780
 INKSVLIFP ELACLNPVL YVFFNFKFE DWKLLKEVT KESSSVSEI SQGSCLEDG 840
 FYIDGMIYSH LQGNLTVCDC CESFLTKFV SKHLIKSIS CPALAVASQ RPBIVSDSCG 900
 35 TQSHSDSTAD EEDSVSDSS DQVQACGRAC FTQSGFPLV RYAINLFRVK D

Seq ID NO: 37 DNA sequence
 Nucleic Acid Accession #: AF146448.1
 Coding sequence: 1..1884

1 11 21 31 41 51
 | | | | |
 40 ATGCTGCGAG CCGCATGTAT CCGCTGCTCT ATCAGGACCT GCCTGCGGGA GGGCACTAC 60
 CCGAGTCCCA TCCGAAATAT CGACTCTCGG TTCTCTCTCG CTGTCGCGCA AGTCGCTCG 120
 AACCTCTTCA ACTCGAAJAA TTGTGCJAAT GAGCTCTGGS TCCAAAGAT TTGCGACGS 180
 GTGCTGTCAA GACAOSATGT CCGCTTGA GA CCGAATTTG GAGTGCGCCG TGTGCTGTG 240
 AGATATCTTA TTTATGTGAC GAGCATTGAA CAGATCTGAG AATGAATAT GACATACAG 300
 ATCCATATGT TTTTTCATCA GACTGAGAAA GATTCAGCT TAGCATACTA TGGACACAC 360
 CTGAGACTGA CCGTGGACJA TGGATGCAAT GAGATATGT GGTTCCTCTA CTGCACTTT 420
 50 TTGAACAGCA AGAGATCTTT CCGCATGTAT GTGACTGTGG AGAATCGCT GTTCAGACT 480
 CACCAGATGT GAACGTGTGG GTACGSCATC CACTCACCA CTACAGGAC TTGTCCCTG 540
 GATCTGCTGA AATCCCATAT GGAACAAGAG CGCTGACACC TGGTGTAGA GAGCTATGCT 600
 TACAGCTGTG AAGACATCAT ATATTCTGGS GATGACATGS GAACGCCAT CCGCATGACT 660
 TAGAGACTCT ATTATCTCTA GTTCACTCTT CTGAGAGAG CATTAATG CAGAGAGST 720
 55 TATTCTTCA CAGGTCTCTA CATACGCTG ATACTGAGT TCCAGGTTCA GAGGAGAGT 780
 AACAGCTAAC TTGTGAGCT CTACTGSCCT ACTGTCTCTA CCACTATTAC CTCTTGATA 840
 CTTCTTTTGA TGAATATAGA TTCTCTGCA GCGAGGTGTA GAATTGCTT AACTTCAGT 900
 CTAATCTTCA CCGCATGCA CCGATGCTG CCGTACAGAT TCCCTGAGT TCCCTGAG 960
 60 AAGCCATTG ATATCTATAT CCGCTGTGTC TTCTCTTG RTTCTCTGCT CTGCTCGAG 1020
 TATGTCTACA TCAACTATCT TTTCTACAT CAGGAGACTC GCGCGAGCCG TAGGSCACAC 1080
 AGGACACCCC GAGAGATCAT TGCCTGCTAC CCGTACAGG AAGTGTGTGT AGGAAAGTG 1140
 CAGATGTGCT TATATACAT GAGACAGCGA GTGACTCTG TCCCATATCA CCGAGCGAG 1200
 GCGCCCTCTG CAGAGCCGGA AAGCTGTGCT TCTTTAGCT CCACTCCGA GCGAGCCGAG 1260
 65 CTGCGCCTCT CGGAAGGCTT CAGCGCCTCT ACTCTCTCT CAGCGCAGCG CCGCTGTGCT 1320
 ACTCGAGAAA CCGTGAAGCA TCTCCCTCT ACTCTGAGG AGCGCCGCGA CAGCTATGCT 1380
 GTCTGCTTTA ATGCTTTTCA GCGTATGAC AGTATTTTT CACCGAAT CCGAGACTCT 1440
 CTGCAAGCTT ATGCGCTGGS TPTTACCAT ATCATATGAG CAGCTATGAG CAGCTTGG 1500
 70 TCGAGAGAG GCGATGGGCA GCGAGCCGAT GCGAGGCCCA TGCTTACCA TCGGAGAG 1560
 GTGTGCGAG AAGCAGGTGT GAGACTTGAT GACACATGAT ACAGAGGCA CTGCTGTGCT 1620
 ATTATGAGC AGTTCAAGT TGAATAGAC ATACTCTGGG GCTTAAATGA TATGAGACT 1680
 ATGCGCCGCT GCGAGAGGA GAGCAGTGC TCGAGCTCT AGGATATG CCGCCAGCT 1740
 CCGGTGCTCT CCGTACGTA AGGCTCTCTC TCGATCTCT TTAATCTGTA CTACCTCCA 1800
 AAGCTGACA AGTGCTCCCG GTTCTCTCTC CCGTCTGCT TGGCTGTGT CAGCTATG 1860
 75 TACTGGTAT ACCATATGTA TTAG

Seq ID NO: 38 Protein sequence
 Protein Accession #: AAD51172.1

1 11 21 31 41 51
 | | | | |
 80 MLRAAVILL IRTWLAENY PSPPKPHPE PSSAVPEVL MLFNENCM EAVVQKILR 60
 VLSRYDLRL PNFGGAPVPV SIIRIVTBIE QISEHNDYT ITWFHTQWK DRLAIYET 120
 LNLTLVRLH EKLAVGCPPI LNSKAPVHD VYVNRVPLQ EPGSTVFQI ELTTTAAKSL 180

PCT/US02/17594

109

PCT/US02/17594

80 Coding sequence: 31..1092

PCT/US02/17594

80

1	11	21	31	41	51	
CAAGCTCTA	AGTAIGCTGC	GACAGACTAT	ACAAATGAAC	TTTATGATGA	CGGAATTAC	60
CTGATTATA	GTCCCTTACT	TCTCTAGTG	GGCATATCCA	TATTAAAGA	ATTAGAGCTA	120
ATAGGAAGT	AGAGTTAAAC	TATAGTTTCA	TTCTTGAAT	TCTTATTTCT	CTTCTTCAG	180

WO 02/098358

PCT/US02/17594

5
 10
 20
 25
 30
 35
 40
 45
 50
 55
 60
 65
 70
 75
 80

TCTTTTCAG TTAACTTACA CACACACACA CACACACACA CACACACACA CACATATGTT 240
 TATAGATGGG ATGGGAGAAC GGATACGGTG ATAAATTAAG GAGTATAGGT TTCTCTTGAG 300
 ATGAJAATGT TCTAAATATG TGATGCGGGA TGCAACCTCT TGATATATTT AAAAGCCATT 360
 GAAATGAJAA AAGGTGTGGG GGAATCCGAA AGGTATAGCA ACCCAACCTT GAGATTTCCT 420
 TGTTTGGGAA TGATTTTTCG ATAACTCTG AGGTATGAAA AACTCAACCT TCTCAACAGT 480
 AGGTCTGAGA AAGGAAGAGA AGTAATTTAT TCTTTATATA AGTAATTTGT AAATATCTTT 540
 TGAACATACC ACTATATGCA ATTTTTCAGT GTCTACATCAT AGTGTATATA TAGGTATCAT 600
 GAJAAAGATG TACTTGTGAA ACTGTCTCA TGTCTCTTCA GAAAAATTTT GCTCTTAAGT 660
 GGTGATCTCA TGTCCTGGTA AATGTTTCAT GAATTTTATT TAATCATPAA AGCTCAACAG 720
 ATTAATAAGT GATCACTATA AATCAAGATC TTCTCTTTGT ACTCTCCCT GTACAGACA 780
 CACAGATCTC CACTCTPACN AQAARATCCA CATGAAJATA GAACTCAGTG TTTTGTATTA 840
 CATAGCTTAT TCAGTACATT TAGAATGATT TTGCTTCCAA TATTCAACCA CAGTAAAGA 900
 CTCAGTACGA ACCGTGTGTG GCGTCTCAGG TTAAGATGAG GGAATATAGA ACTGAGTACG 960
 CAGCTCCAGG ATCGAAJAAA CGTTTTCCCA AGCGTGGGA AGCGTGGGA ACTGTACCA 1020
 CAGTCTACT GAGTGTGAAA CTTCTTTAAG MCGCTTTGG GTCTCTTGCT TCTGACATC 1080
 TGGATCTGAA AAGCATCTTA CTAGATGCTT GGGATACAT GAAGCTCTTG TGAACAAC 1140
 TTTTCTCTTG TTTTGTCTAG CTCTCTTGAG AGTCCATTC GGAAGCAAG CAAATGCTCT 1200
 GTGGAJAAA GGGGCTCAGG CTTCTTTG TGAAATCTGG GAJAAAGCT GGGTGTGG 1260
 TTGACAGAGA TGTGCAACCG CAGGCGCAGG ATCATTTCC AGCGACAAA ACAGCATTTG 1320
 CAGCTCAAGG CTCACACTGG GGAATTTGCT ATAAATGAGA AGCTGATGCG AGAGAGCTA 1380
 TGTGCTTCCA CTGAGCTTGT GATACTCAT TTTCAAGTGT TAATGAAA CCCTTTAGAA 1440
 ATATTTGAG CTGAATGAG GGTCAATGAT ATAAATGAGC ATCTCTCGT GTTCACTGAA 1500
 AAGGAATGAA TTCTAAARAT ACCGGAARAC AGTCCCTAG GAACTGAGTT CCGCTGAAAT 1560
 CATGCTTTGG ACTTGGACGT AGGAGCAAT AATGTTCAA ACTATANAAT CAGCGCAACG 1620
 TCTCACTTCC GGGTCTTAAT CCATGATATC AGMAATGAGA GGAATATACC TGGCTATGTT 1680
 TGTGATTAAG ACTCTGATCG GAGCGGGGAG CCTCACTGA ACTCAACCT CAGACGCTT 1740
 GAGGTGCTG TCTCAACCGG ACTTGAACAT GCTCAAGTCC GATTTAGAT GGTGAGCATC 1800
 AATGATTAAG CTTCTGAGTT TGACAGATCC ATCTCAAAJ TGCAAGTTC AGRAAGACGT 1860
 CCTCTTGGCT CCGTGTGGC CAGCTCTTCC GCGCAGGATT TAGAGCGGGG AGCAATGGA 1920
 AAAATATCAT ACACATCTCT TCAAGCTTTC GAGATATTA TGAAACTTT GGGATTAAT 1980
 CCTATGAG GGAATGAGAG ACTGTGAGAG CAGTGTGAT TGAATATCT TACTTTCTAT 2040
 GAGTGTGCA TCAAAAGCAC AGATGGGGGA GGTCTTTGAG GAATATGAC TCTTCTCTG 2100
 CAGTGTGTGG ACTGGAATGA CAATCCGCGA CAGGTGACCA TGTCTGACAT CACAGACGCC 2160
 ATCCGAGAAA GGTGCTCTGA GAGATGAGT GTGCTTTTCA GGGTTCAGA TCTTGAAGCT 2220
 GGAACAGTA GGAAGAGATC TCTCTCTCAT CAGAGAGC TCTCTTTCT TCTAAATCT 2280
 CTGACAGAGA ACTTTTACAG CTGTGAGAGT GAGGAGGAC TCGACAGAGA AGCAGAGCT 2340
 GAATATAATA TCACCTCTAC CTCAAGAT ATGAGGAGTC CAGGCTGAA AAGAGAGCAC 2400
 AACAATACAG TCGAATATCT AGATGTCAAT GATAAGGCC CCAGTTTCAC CAAAGCTCT 2460
 TACAGCTTCT GAGTCAACAG GGTCAACAGC CCGGCTGAC AATGTGCGAG CTGACAGCC 2520
 ACAGACAGAG ACTCAAGCAC CAGCGCCAGG GTCACTCATG GCTGTGTCG CCGCCAGAGC 2580
 CGCGACCTGC CCGTCCGCTC CCTGGCTCC ACTCAAGCGA ACAGCGGCCA CTTGTTGCC 2640
 CTCAGCTGCC TGACATGAGA GCGCTCGGCG GAGTTCGAGT TCGCGTGGAG GCGCACAGCT 2700
 CGCGCTGCC CGGCTTGAG CAGCGAGGCT CTGTGTGCGT TGTGTGTGCT GAGCGTCAAC 2760
 GACAGCTGC CTTGTGTCT GTACCTGCTG CAGAACGCGT CGCGCTGCTG CAGTGGATG 2820
 GTGCCCGCG CGCGCGAGCC GCGCTACTGT GTGACCAAG TGGTGGGGT GAGCGCGAC 2880
 TCGCGCGAGA ATCTCTGGCT GTCTATACAG CTGCTCAAG CAGAGAGCG GCGGTGTC 2940
 GGTGTGTGG CCACTAGT GAGGTGCGC ACCGCAAGC TGTGAGGGA CGCGAGAGCA 3000
 CCGAGAGCA GGTGTGTGT GTGCTGAG GACAGAGG AGCTCTCG GTGCGCAC 3060
 GCGAGCTGC AGTGTGCTCT GGTGAGGCGC TTCTCCAGC CTTCTGTGCT GCTCCAGAG 3120
 GCGCGCCCG GCGAGGCCA GCGCACTGT GTCACTGTCT ACTGTGTGT GCGTGTGCC 3180
 TGGTGTGTCT GCGTCTCTCT CTTTGTGGTG GTCTGTGTGT TGGCTGTGTG GCTGTGAGG 3240
 AGGCGAGG CGCTCTGGT GCGCTCTC TCGATGCTG AGGAGCTT TCGAGGGGT 3300
 CTGTGTGAGG TAAGCGCAC GCGGACCTGT TCGCAAGCT ACAACAGA GTTGTGTCT 3360
 ACAGAGGCT CAGAAACAG TGAGTTCAAG TTCTGTAGC GATATGCC CAACTCTCT 3420
 CCTTAGGCA CTAGAGAGA AATGATTAAT AATTCACCT TCAACATAG CTTTGATTT 3480
 AATTTGAT AGAAGCAT CTGTATAT CTATGATCT AATGATCT CTATGATCT 3540
 CTGTATTCA TGTCAACCA CACCAATAAG GATTTTCT CTATGTGTTA CTTCMAAT 3600
 TATTTTAAT TCGATTTCC CTTTCTCTCA TATTTAACC GAGAGGTGT TGCATATAGA 3660
 ATCGAAATTA ACAAATATA CTTTACTTC AAGGTGATG TGATTAATA TTTTTCGCT 3720
 TTTTATTTT ATTAATCTC TATTTATTT TGTGATGAT TTTCAATTA CTGTATGAT 3780
 TCTGTGAT TCAACATTA AATCAATG TGTGATGAT TATGATGAT TATGATGAT 3840
 CATTTCTTT GTCTACTCT CTTCAAAAT TGGTATTTT GTTGGCTCA ATTTCAATTA 3900
 TATCTTTT CTGAAGTTT CTTCTTCTT TTTTCTTCT TCTTTTCTT TTTTTCCTT 4020
 TTTGAGAG GGTCTTATCT TTTGATCTA GGTGTGAGTG CATGAGACA ACTTGTGCT 4080
 ACTCAACT GGTCAAGCT GTTCAACAG GGTCAACAG GGTCAACAG CAGTGTGCT 4140
 GBACTTAGG TCGATGCA CAGTCTTGG TAACTTTTG GAGGATGAG ATTTTGCAG 4200
 GTTGGCAGG CTGATCTGA ACTCTGGGCT TCAAGGCAT CTCTCTCTC AGCTCCCCA 4260
 AATTTGCGA TTPACGGCAT AAGCAATGT CCGCCGCCA AGTTTATTT ATTTATTTT 4320
 TTMAGAGG GATCAAGCT GTTCACTTTA AAAAAGATC ATTAATCTA TGTATGCT CTGTATGAT 4380
 AATTTCTTAA ATAAATAA ATATTCTTA TGTATGATG ATGAGAACT TTTTAAACGC 4440
 CTATCTTAA AATAAAGCA GAAGCCATG TAAGCATTC AGTATGTGA AATGTTGTT 4500
 TTTTGTAGA CAAJAGGCA AGGTATATG TAAAGATTT TATATATTA TTTTCTTAT 4560
 TATCAATTA AATAAGAT GGTGCGGTT ATATTTTAT TGTCAATTA CTCAATCT 4620
 TTTATGTTA AAAAAGAT ATCAAAGTA CATTTACT GTTGTGCTT TATATCATC 4680
 ATAGTATA TTTGCGGAT CTAGCCCTTT CTTCTGAAA TATCCATG TTTTATCTG 4740
 ATTTCTGCT TATTATATG AAGTGTAGC TTTCTTCTAG ATATTAGCC TTTGAATTA 4800
 ATTTATATG AGTCAAAA AAAAAA

Seq ID NO: 48 Protein sequence
 Protein Accession #: NP_066008.1

1 11 21 31 41 51

WO 02/098358

PCT/US02/17594

5 NEIGHNRRR ORQLVFFVL LSLSCAGAEI QYYSVVEITE RSGPVANLCK DLGLGLETMS 60
 TRKRIISQO HQHQLQKQO DRELLINERL DREELCPSE FCLHIFQVLM INFLRIFQAR 120
 LRVIDINRHS MPPEKIMVL KIPENSPLGT EFLIMHALDI DVGRRNVQNY KIPSESHFVR 180
 LLIHBFDRQI YPELVDLKE DRESEPLRL TLIALDQSGP PRSGTAQVRI RVDVINDNAP 240
 EBEQPIYKQI IPENIFLOGL VACYSARELD QANQKISTT LFPQSEDLK LLEVMPKGTG 300
 VLRKQVFE WYTSYERIK ATIDGLSLCK CTLLQVQVY NRPQVYMS ALTSYIPERS 360
 PETIVAVFSV SDPDQBNK TISIGDQLP FLKPSVWNP TTVITERALD REBAYENIT 420
 LTVTDGWR LKTEHITVQ ISDVNDNAPF PTQTSYFLV RBNNSPALJI GVSATDRDS 480
 10 QTNQVQYSL LPQDQPHLP ASLYSDNACN GHFLALSHLD THAEKSEFER VSAIDRQSPA 540
 LRSBALRVIL VIGADNNSFP VLYPLQWGA FCFBLUPRAA EFCVYVTVV AVDSKSGA 600
 WLSYQLLEAT EPGLFGWAL NQRYPARLL SBRDAAQRL VVLVNDNOSP PRSACATLHV 660
 LLVDGQSQPF LPLFEAPQO TQANSLTYVL VVALSVSSL FLVSVLFLVA VLCSRERAA 720
 SVORCSNFBG PFPQRLVDVS QVTTLQSQSY YZVCLTGUSE TSEFRLKPI IPMFSP

Seq ID NO: 49 DNA sequence
Nucleic Acid Accession #: CAT cluster

20 1 11 21 31 41 51
 TTTTTTTTTG ATAAATGACA GACTTTAATT AAATCTGTAC TAAATTTAAA TGTCTAAATA 60
 AACTTGAAGT GTACATGATA CATCTAAATG TATCTTTATA TATTTTATT GTGCATTTTA 120
 TCTCAAGGSG TCTCTTTTGT TAGGTGTATA AAGCTTTCTT ATTTTATATA TAATYATAGA 180
 25 TACTTCAAT AAGAGAAATC CACACCAATG AATACATAGA AGAACATAT ACTTATATC 240
 AAGCAAACTA AAATGTGTCA ATCTCTAAOC ACATGAACCT TGTATTATT GTACAGCATG 300
 TACAATGTT ATGCTTCACA GGGTGAAGTA GAGACTCOAA AACTTGAAC CTGGGACAAA 360
 TAGAGAAATA AGGAAATTT CACACATAT TATATATTATA GAAATGTGT ACTTAAACAG 420
 TTAGATACAA AGTGTGAAA AATGHTAGTA TTTAGTGGGA TCTAGAAAT TTA

Seq ID NO: 50 DNA sequence
Nucleic Acid Accession #: AF034799.1
Coding sequence: 170..394

35 1 11 21 31 41 51
 GATCTGGGGA GGCAGTGTG GAGACGAAT CTCTAGCTCT CTTCACGGC TCCACGAGG 60
 GAACGGCTGC AGGAGTCTG GCTGTGAGCC TCCCTCTCC TCAAGCCGGA GACGCCGCTT 120
 GTCATTGATC AATTGAAGAA CAGAGGACCC GAATACACAG ACATTAGCAA TGAATGTGTA 180
 40 AGTGAGGCC AGGTTAATG AGGACACCCC AATGAGCCAA AGGGGGTCCC AAGCATGTGG 240
 CTCGAACTCA GACTCCCTT TTGAGCAAGT GATGTTGAAT AGCTAGATAG AATAGGAGTCG 300
 TCTTCGAGAG CACGACCGAA GAGCTCTCCA CTCTCCCACT CTCTCCCACT GAAGACITCA 360
 GGAATGTCTC TATGACCGAG ACTGCTCTCA GAGACAGCTC AATCTGCCCC TCCACACAGA 420
 TATCGAATCC CTACACAGAG GGTCTGCTGCG TTCTAAGGGG GCTGATCCGC CGGAATTTCC 480
 45 TGACATGACA AAGAAATTGA ATGCTCCGAG GGAACCACTT CTAGAAAAGG AAGRAMAAAT 540
 CTCCTGACTT AAGCTGAAA GAAACAGCC AAGCATTTA CTGGAGCTT TGAGTACCTT 600
 TGCTGTACGA CATGAAAGT CACTAAGAA AGCCTTGATA AAGCCGCAAG CCGAGTCTCC 660
 CTCAGAGATA TCCAGTGAAG TTGAAGTTCT CAGGCACTG AATCTTTGT TTGAGCACCA 720
 CAGGCGCTTG GATGAAGAAG TAAGCGAGCG ACTGAGGAGT TCTTTAGAAA GAGTCTCTCC 780
 50 ACTGAGAA GAAGTACGTC CTCTCATCTA GAGATATGTT GCTTCCGTG ACGAAATGTT 840
 TCACTATCCA AGAAATAATG CACTACAGGA GAGTCCACA GATCACAGAC ACTCTGAGAG 900
 CATGGAACCT GGACAGAAAG TCAATGAGAA GGGTTGTCC AACGTTCTA TGACTCTAAC 960
 CGATGAACCT ATGTAAGAAG TTGAACTACA AGAATGTGCT GAAGAGAAA ACTATGAAT 1020
 GGCCTGAGTG AAGAAAGCTT TAGCAAGCTT TTCTTCCGGA ATGAGGAGG TGGACAGAGA 1080
 55 AGACAGCA GAGAAAGTCA ACTCTATTAA ACAGTATGAA ATGACACCA CTCTAGAG 1140
 GAGCAATGAG GAGGCCATG GACAAAAGGA AGATATGAAA AAGAATTA CAACCTGTGA 1200
 AAGGCTTTAC CTGAGTGTCT AGAGAGAATC TACCTCCATA CATGACATGA ATGATAAAT 1260
 AGAAGATGAG TTGAGCAATA AAGAACTAT CTATGGGCGG ATGAGAGAGA AAAAAACAA 1320
 60 CTTCAGAA CTTCTTGAGC TAGCTGAGA AAGATTGCGA GAGACAGTA GAGAGCTCA 1380
 AAGCTGCCCT GAGGTAGAGG CTGAAGTGC TCAAGAAATT GCAGGCTTAA CGAGCGTGA 1440
 GAGCTACCAT GAAATATTG AAGAACGTAT GAGACATTTA GAGGCTCAAC TTGAGAGAAA 1500
 GATCTAGAAA CTCTCAAGAG ATGAGCAAG AGGAAATAG AATGAGGAG ATACACAGAG 1560
 65 ATGATGAT ACCTGTGACA GACTCTGATG TATGCTGATG GAGGCCCTCA ACTCATGCT 1620
 CTGATGAAGA ATGCTCTGCT TAGAGAGAAA GAATGTTTTA ATTGAAGAT GAGAACTTT 1680
 CAGAAAGAA CTGGAAGAA CTCTACATGA TAAGGAAGCG TTACAGAGAG AAATGTAAA 1740
 GCTGAGATCT GAACTTGACC AATCTCAAAAT GAGCACTGAC TGTTTAATTG AACCCAGAT 1800
 70 ACAGCAACT CACTGAGACA CTCTCACTGA GTTCCGATAC TGTCTGAGCT GACTAGAG 1860
 GCTGAGCTCT GATTACAGCA CACTATTAAT TTGATGAGG ATGAGAGGA CTAGGCCCTG GCGCCATG 1920
 TGTGCCAGGA GATCAGGCAA AGGTCAAAATC TCTTGCGAT CAGAGATGGA ATGAACTGA 1980
 ACAGATGGGA GTACTAAGCA GCCACCTTTT AGGAGGTGAC ACTGAAATGT CTGATATTGA 2040
 TATGTGTGAC AGGAAACAAA TTTTTPGCTT TGAAGATCTT CTCTCTGAAA GTGTGATCT 2100
 75 GATGTCCG AGGATGATCA TATGCTCTCA GACACATGAT GAGGCCCTCA ACAGAGAT 2160
 GAGCTGAT CTGAGAGAAA AAGATCTCAC AGGTGTGCT GCTGAGAGAA TTGAAATAG 2220
 ATGTGCTAGT GTGAGCTCT AGGCCCTGAA TTGCGCAATG GTGACCCAG GTACTCTCAT 2280
 TACGCCCTCT GTTACAGCT CATGCCGTGC GAGTGTATCT CCCCAGAGT GACACTGAC 2340
 80 TCGAAGCTCT ACTCTGAGCA CCGCTCCGAG GCGAATGAG CTCTGAGCT TCTGAGCT 2400
 GAGCAATGAT CTGAGCAATC GTGAAAGAAA GATTCGAT TTGAGAGAT ACTGTCGAGA 2460
 GAGCAAGACA ACAATTAAT GTGAAATCTC TCTCTCTCT ACCCTGAGG CCTCGAGAT 2520
 GAGTCAACT CTCTCTCTCT GTGACACAAA TATGCTGCGA AGTACCTTAT CTCTCTCTCT 2580
 TAGGCTGAGA AGGCTGAGCA TATGCTGAGT GAGTCTGAGT GAGGCTCTCT TTACAGCT 2640
 CCGCAAGAG AAGGAAATCA ACTCTGAT AGCTCTCTCT TTGTGTAAA AAGAAAGAG 2700
 TCGATCTGG GAGCTCGAG GCTTTATGCA GACTCAAGCT GCGCTCGAG AGTCCCTGG 2760
 GTTAGCCAAA CTGCGAGAT GAGCTGAGCA GGTGCAAGGA CTAAGAGAAA AGCATGAAT 2820
 TCTTGAAGAA CCTCGAGCAA AGGATTAAC TTTCCTCAG TGTGRTGAG CACTGTGTGT 2880

PCT/US02/17594

Seq ID NO: 51 Protein sequence
Protein Accession #: AAC26100.1

203

It is understood that the examples described above in no way serve to limit the true scope of this invention, but rather are presented for illustrative purposes. All publications, sequences of accession numbers, and patent applications cited in this specification are herein
5 incorporated by reference as if each individual publication or patent application were specifically and individually indicated to be incorporated by reference.

WHAT IS CLAIMED IS:

1. A method of detecting an androgen-independent prostate cancer cell in a sample from a patient having undergone androgen ablation therapy, the method comprising determining the presence or absence of a nucleic acid comprising a sequence at least 80% identical to a sequence as shown in Tables 1A-4.
2. The method of claim 1, wherein said determining is by hybridizing with a polynucleotide that selectively hybridizes to a sequence at least 95% identical to a sequence as shown in Tables 1A-4.
3. The method of claim 1, wherein the biological sample:
 - a) is a tissue sample; or
 - b) comprises isolated nucleic acids.
4. The method of claim 3:
 - a) wherein the nucleic acids are mRNA; or
 - b) further comprising the step of amplifying nucleic acids before the step of contacting the biological sample with the polynucleotide.
5. The method of claim 2, wherein the polynucleotide:
 - a) comprises a sequence as shown in Tables 1A-4;
 - b) is labeled, including a fluorescent label; or
 - c) is immobilized on a solid surface.
6. The method according to claim 1, wherein said biological sample is contacted with a plurality of polynucleotides that each selectively hybridizes to a sequence at least 95% identical to a first sequence as shown in Tables 1A-4.
7. The method according to claim 6, wherein said plurality of polynucleotides are immobilized on a solid surface.

8. An isolated polypeptide which is encoded by a nucleic acid molecule having polynucleotide sequence as shown in Tables 1A-4.
9. An antibody that specifically binds a polypeptide of claim 8.
10. The antibody of claim 9:
 - a) further conjugated to an effector component, including a fluorescent label a radioisotope or a cytotoxic chemical; or
 - b) which is an antibody fragment or humanized antibody.
11. A method of detecting an androgen-independent prostate cancer cell in a patient having undergone androgen ablation therapy, the method comprising contacting a sample from said patient with an antibody of claim 9.
12. The method of claim 11, wherein:
 - a) the antibody is further conjugated to an effector component, e.g., a fluorescent label; or
 - b) said sample comprises a cell.
13. A method of detecting antibodies specific to androgen-independent prostate cancer in a patient having undergone androgen ablation, the method comprising contacting a biological sample from the patient with a polypeptide encoded by a nucleic acid comprising a sequence from Tables 1A-4.
14. A method of inhibiting proliferation of androgen-independent prostate cancer cells in a patient having undergone androgen ablation therapy, the method comprising administering to the patient a therapeutically effective amount of a compound that specifically eliminates cells expressing an antigen listed in Tables 1A-4.
15. The method of claim 14, wherein the compound is an antibody.
16. A drug screening assay comprising the steps of:

- a) administering a test compound to a mammal having a prostate proliferative condition or a cell isolated therefrom;
 - 65 b) comparing the level of gene expression of a polynucleotide that selectively hybridizes to a sequence at least 80% identical to a sequence as shown in Tables 1A-4 in a treated cell or mammal with the level of gene expression of the polynucleotide in a control cell or mammal, wherein a test compound that modulates the level of expression of the polynucleotide is a candidate for the
70 treatment of prostate cancer.
17. The assay of claim 16, wherein:
- a) the control is a mammal with prostate cancer or a cell therefrom that has not been treated with the test compound; or
 - 75 b) the control is a normal cell or mammal.
18. A method for treating a mammal having a prostate proliferative condition or prostate cancer comprising administering a compound identified by the assay of claim 16.
- 80 19. A pharmaceutical composition for treating a mammal having a prostate proliferative condition or prostate cancer, the composition comprising a compound identified by the assay of claim 16 and a physiologically acceptable excipient.
- 85 20. A method of detecting a prostate cancer associated transcript, the method comprising contacting a biological sample from the patient with a plurality of polynucleotides wherein at least two of said polynucleotides selectively hybridize to a difference sequence at least 80% identical to a sequence as shown in Tables 1A-4.
21. A method of detecting a prostate cancer, the method comprising the steps of:
- 90 a) providing a biological sample from a patient;
 - b) contacting the biological sample with a first polynucleotide that selectively hybridizes to a sequence at least 80% identical to a first sequence as shown in Tables 1A-4, to determine the level of a prostate cancer-associated transcript in the biological sample; and with a second polynucleotide that selectively

- 95 hybridizes to a second sequence at least 80% identical to a sequence not
shown in Tables 1A-4; wherein the expression of said second sequence is not
substantially changed in prostate cancer, to determine the level of expression
of a control transcript in the biological sample; and
- 100 c) comparing the level of the prostate cancer-associated transcript to a level of the
normal tissue associated transcript in the biological sample.

22. A method for quantitation of a prostate cancer-associated transcript in a cell from a
patient, the method comprising contacting a biological sample from the patient with a
polynucleotide that selectively hybridizes to a sequence at least 80% identical to a sequence
105 as shown in Tables 1A-4.

23. The method of claim 22, wherein:
- a) the polynucleotide selectively hybridizes to a sequence at least 95% identical to a
sequence as shown in Tables 1A-4;
- 110 b) the biological sample is a tissue sample;
- c) the biological sample comprises isolated nucleic acids;
- d) the nucleic acids are mRNA;
- e) further comprising the step of amplifying nucleic acids before the step of
contacting the biological sample with the polynucleotide;
- 115 f) the polynucleotide comprises a sequence as shown in Tables 1A-4;
- g) the polynucleotide is labeled, including a fluorescent label; or
- h) the polynucleotide is immobilized on a solid surface.

24. A biochip comprising a plurality of polynucleotides that selectively hybridize to a
120 sequence at least 80% identical to a sequence as shown in Tables 1A-4.

25. A method of screening drug candidates comprising:
- a) providing a cell that expresses an expression profile gene selected from the group
consisting of an expression profile gene set forth in Tables 1A-4 or fragment
125 thereof;
- b) adding a drug candidate to said cell; and

- c) determining the effect of said drug candidate on the expression of said expression profile gene.

130 26. A method according to claim 22 wherein said determining comprises comparing the level of expression in the absence of said drug candidate to the level of expression in the presence of said drug candidate.